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CONTENTS

SUPPURATIVE PERICARDITIS WITH CALCIFICATION OF THE PERICARDIUM AND EPICARDIUM

HOWARD LILIENTHAL, M.D.

The patient, John J. T. (Adm. 332702), a man aged 54 years, was sent to me by Dr. Philip Corn of Floral Park. About two years before I saw the patient he had what he thought to be a cold, and at that time his heart was said to be "not perfectly normal". But after this, in fact in January 1930, he was accepted as a normal risk by one of the best life insurance companies. Toward the end of 1930, the patient noted a gradual weakness accompanied by shortness of breath following exercise. At that time, although he weighed 170 lbs., there had been loss of weight and loss of appetite. After this there was moderate cough and slight blood-stained expectoration, but the sputum had never been purulent, nor had there been any sign of tuberculosis. Then he noted that his abdomen was beginning to enlarge, and in March 1931, he consulted Dr. B. S. Oppenheimer who made the diagnosis of Pick's syndrome. Salyrgan was then administered with some improvement in the edema and ascites. Gradually the patient became obliged to spend his time in bed. During the six weeks before he entered the hospital the renal output had greatly diminished.

Late in November 1931 he entered the Private Pavilion of The Mount Sinai Hospital, where I first saw him. My first impression of this patient was favorable. He did not look ill. But his abdomen was ascitic, and when he sat for a time in bed, the ascites diminished and the legs became edematous.

November 29, 1931, about eight months after Dr. Oppenheimer's first examination, he went over the patient again, in the hospital. He found the blood pressure, on the right, 90 systolic and 60 diastolic; on the left, 88 systolic and 58 diastolic. The circulation time (decholin), 14 sec. recumbent; 16.5 sec. sitting. The urine contained no albumin nor sugar, and the specific gravity was 1.020. Venous pressure, 13.5 cm. X-ray examination by Dr. Jaches revealed a heart not greatly contracted, but with what he diagnosed as an enormous deposit of lime in the pericardium. The right chest contained fluid up to about the middle (Figs. 1 and 2). There was no fluid in the left chest. This phenomenon, according to Dr. Oppenheimer, is frequently observed in Pick's disease. The quantity of sputum was from 3.5 to 4.5 oz. a day, and the patient stated that it dimin-

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ished when he did not smoke. Its quality was mostly salivary and mucoid—no pus and no acid-fast organisms. With the diagnosis of calcified pericardium, which interfered greatly with the action of the heart, Dr. Oppenheimer and I agreed that an operation to relieve the heart-strain was advisable, and on December 1st I carried out the procedure. Dr. Branower administered a minimal dose of avertin, and the anesthesia was continued with a little nitrous oxide and very little ether. The blood pressure was noted at intervals during the operation, so as to give warning of danger. Dr. Ira Cohen acted as first assistant, and Dr. Corn and Dr. N. Cherwin were observers.

Fig. 1. Case of John J. T. Calcified pericarditis; considerable fluid in right chest.

The Operation. Electric surgery was not employed in this case because of the proximity of the heart. I had heard of instances in which death from cardiac shock had resulted apparently from static electric influence.

An incision was made with a scalpel from the level of the third rib down the median line of the body to a point half way between xiphoid cartilage and the umbilicus. Then the sternum was cut across with Hudson's forceps at the level of the third interspace. My left index finger was gradually forced behind the xiphoid cartilage along the posterior surface of the sternum as far as it would go, and the xiphoid and sternum were divided sagittally with the aid of Schoemaker's sternum shears, an excellent instrument (Fig. 3). It shields the parts beneath and cuts the sternum with facility and without sudden closure which might be shocking. I have employed these valuable shears in several cases, and always with satis-

faction. The incision through the bone was carried up to the point of its cross section, dividing the posterior periosteum all the way. The motion of the lungs within the pleura was clearly visible at each side, and the pleurae were easily avoided. With the scalpel the abdominal part of the incision was now opened and the diaphragm cut with scissors. The pericardium with the characteristic feel of dense calcification was clearly manifest to the palpating finger, and then with the scalpel the pericardium was entered, the halves of the sternum being held apart with sharp re-

Fig. 2. Same case, lateral position

tractors. With a heavy scalpel the calcified anterior part of the pericardium was slowly divided, and there was a sudden gush of opalescent fluid from within. Cultures were made because it had entered the peritoneum as well as spilling into the wound in every direction. At first I thought that this exudate came from the right pleura, but on enlarging the incision I could easily appreciate the calcification of the visceral pericardium and also the calcified pericardial sac. The pleura had been nowhere entered. It was quite evident that the disease must have begun

as a pericarditis with effusion.   It seemed almost impossible that the heart could have maintained any circulation, feeble though it was, in these circumstances.

The opening in the pericardium was now enlarged so that eventually two rib-spreading retractors could be inserted and the right ventricle and auricle were now clearly seen.   The pericardial lime deposit, although very hard, was not thicker than a piece of blotting paper, and in many places
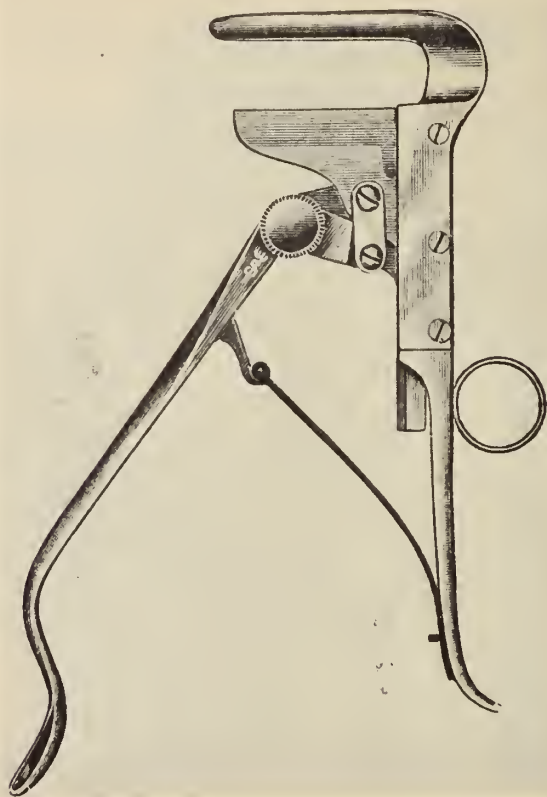
Fig. 3. Schoemaker's sternum shears

more nearly resembled the shell of a guinea hen's egg.   A small area, about 1 cm., of the lime coating was removed from the heart wall with scalpel, fine forceps, and sharp raspatory.   Then pieces of this eggshell encasement could be bitten out with a small rongeur.   Eventually about six square inches were removed and the pulsation of the heart forced the walls of this organ forward, releasing it to a considerable extent.   Dr. Oppenheimer believed that it would be wise to rest satisfied with this amount of cardiolysis at present.   Should the patient make a good recovery

it was suggested that another operation might be performed to remove still more of the lime casing. The problem of exactly what ought to be done at the second stage, if there should be one, was rather complicated, and would have to be further discussed. The blood pressure at one time rose as high as 100 systolic and the condition did not appear to be bad. There was oozing, most of which came from the incision and not from the heart muscle. The wound was closed, the abdomen and diaphragm being sutured with interrupted chromicized catgut stitches; then the external layer of the calcified pericardium was drawn together with some sutures, leaving a small space next to the diaphragm through which a special porous drainage tube was inserted and left in place so as to avoid cardiac tamponade by blood or serum. During the operation there was discharge of ascitic fluid which was taken up by suction. No sutures were placed through the sternum, but the soft parts were drawn together with silk-worm-gut. The patient stood the procedure well, and about eighteen hours after operation the general state seemed excellent. His blood pressure was 106 systolic and 70 diastolic.

On the second postoperative day, 1400 c.c. of perfectly clear fluid were aspirated from the right chest. The temperature had not risen higher than 101°F., and the regular pulse did not make the impression of tension as low as the sphygmomanometer indicated. Two and a half days after the operation the readings were: left, 90 systolic and 62 diastolic; right, 106 systolic and 70 diastolic. The tube was removed because drainage was insufficient through its porous structure, and was replaced with a smaller one of the ordinary type. Through this there was a free flow of seropus rhythmically with the respirations. It was fitted with a finger-cot valve. The patient's morale was excellent, and his respirations easy although there was increased cough.

On December 15 I made a note that six days postoperative, digitalis was administered but that instead of reducing the number of cardiac pulsations their rate had risen to 136 and the pulse had become irregular. The tube was removed and the wound opened as far as the pericardium to facilitate discharge. Bronchopneumonia with increased cough and expectoration made it necessary to resort to an oxygen tent. This, in a measure, gave subjective relief, but there was progressive deterioration with mild delirium. Great postural edema appeared and death occurred two weeks after the operation. Noteworthy is the fact that the kidney function was but slightly impaired, and that there was free flow of urine up to the time of death.

This case has been presented because, so far as I have been able to discover by a reasonable survey of the literature, it appears to be unique. This is not the place to discuss Pick's syndrome, nor even pericarditis as such, except to call attention to the well-known differences of opinion on the priority—the polyserositis or the pericardial thickening.

Thoracic surgeons will know that pericarditis is more common than is generally believed, and that the x-ray appearances are not always sufficiently striking to arouse suspicion of its presence. There can be little doubt that the mere fact that pus is present in a location which is ordinarily considered particularly dangerous, too often delays operation or even surgical counsel. I am convinced that it is this postponement which conduces to calcification. One may also conclude that in the more malignant infections in which surgery has not been invoked, death will end the case before calcification appears.

In this report, it will be noted that we were dealing apparently with an organism rarely encountered in pericarditis, namely the staphylococcus albus, which we may regard as of very slight virulence. The outstanding condition which makes this case most unusual and perhaps the first to be reported, is the calcification of the two layers—both pericardium and epicardium—with no adhesions between, and with a considerable quantity of pus between the layers. It may well be realized that the peeling away of the calcified epicardium, even though its thickness be only that of an egg-shell, is fraught with grave danger to the branches of the coronary vessels. Were I to be confronted with another problem of this kind, I would be inclined to divide the operation into two stages: first, the removal of as much of the external pericardium as might seem safe and then, after a few days of interval, to operate upon the epicardial layer. I am well aware that this would defer the actual release of the heart; but I fear that to attack the epicardium first and then to be obliged to postpone the remainder of the operation might be more liable to result in adhesions than would be the case if the true pericardium were to be primarily resected. In my case the purulent fluid had made a space large enough to permit more than normal diastole. After all, if the patient has gone as far as this one had, and yet had retained sufficient vitality to permit of any operation, a delay of a few days between my proposed two stages would seem not too dangerous. I would emphasize the necessity for pericardiectomy in spite of the space referred to, so as to get rid of the rigidity of a membrane which normally is very thin and flaccid.

As to the cause of death in such cases, it should be recalled that a number of patients have been reported dead after an apparently successful operation, from causes never determined. Arthur M. Shipley of Baltimore, who has contributed much to the surgery of pericarditis and who has made an extensive study of the literature, has written me that he has never heard of a case similar to the one here described. His latest article appears in the Annals of Surgery for May, 1936. There is an appended list of references which may interest the reader.

A QUADRUPLE KIDNEY WITH A HORSESHOE COMPONENT DEMONSTRATED WITH THE AID OF EXCRETION UROGRAPHY

MOSES SWICK, M.D.

[From the Surgical Service of Dr. Edwin Beer]

An unexplained elevation of temperature, a persistent pyuria, or an obscure abdominal mass may frequently present diagnostic difficulties. Accompanying outspoken urinary symptoms or signs are a definite lead. On the other hand, the symptoms or signs may be predominantly of a non-urinary nature. Then they may present a difficult problem for diagnosis.

Because of inherent difficulties and inconveniences associated with cystoscopy and retrograde pyelography in children, the physician has been frequently inclined to dispose of a case of pyuria with a diagnosis of pyelitis, or to remain in the dark regarding the nature of an unexplained fever or of an abdominal mass. In the diagnosis of such obscure conditions, excretion urography may be of considerable aid. With its more frequent application, the status of the urinary tract in general is often revealed with greater accuracy, and congenital anomalies are detected more frequently, especially in children. However, it is not implied that retrograde pyelography plays a minor rôle in children, and that excretion urography is not without its limitations, nor is it suggested that the latter can supplant cystoscopy, retrograde pyelography or ureteral catheterization. However, as additional means in the urologic armamentarium, it has frequently helped in the solution of diagnostic problems when considered in conjunction with the history, physical and laboratory findings.

Excretion urography has been particularly helpful in the detection of obstructive lesions of congenital origin or lesions produced by inflammation or any obstructions, when superimposed upon congenital anomalies of the urinary tract. Children with pyuria, erroneously attributed to pyelitis, have not infrequently been found to be suffering from conditions such as (1) secondary infections superimposed upon a malformation of the urinary tract, or (2) urinary tuberculosis, or (3) calculous pyonephrosis, or (4) urinary retention due to contracture of the neck of the bladder. The diagnosis of pyelitis should therefore be made only after the pathologic condition in the urinary tract is definitely recognized.

The following case illustrates the value of intravenous urography in detecting a very rare congenital anomaly—quadruple kidney with a horseshoe component.

History (Adm. 345360).   A twenty-one month old female was admitted
to the Pediatric Service of the Hospital on March 14, 1931 with the
following history: several months prior to her admission to the hospital,
the child had had pyuria accompanied by intermittent bouts of elevated
temperature, irritability and poor appetite, each lasting for several weeks.

FIG. 1. Intravenous urogram in a two year old child.   Quadruple kidney with
horseshoe; an apparently normal right upper urinary tract (A); a normally ro-
tated left upper pelvis which appears stunted (B), as seen in a double kidney;
right half of horseshoe kidney (C); dilated pelvis and ureter of left half of horse-
shoe kidney (D).

Examination.   The child was well developed but pale.   The spleen was
palpable; the kidneys were not.   The urine showed 2 plus albumin and
numerous clumped white blood cells.   The urine culture revealed B.
Alkaligenes and a gram-positive coccus.   The blood findings were: hemo-
globin, 54 per cent; red blood cells, 4,000,000; white blood cells, 10,000, of
which 86 per cent were polynuclear neutrophiles; the blood urea was 13 mg.
per 100 c.c.   An X-ray of the abdomen showed no evidence of urinary
stone.   Toward the end of the fourth week in the hospital, the child

developed an intense swelling in the right cheek with edema reaching the angle of the mouth and lips. Because of the suspicion of mumps, the child was sent home to return at some future date for additional work-up.

She returned twenty months later for further investigation and was admitted to the Surgical Service. At this time, the examination revealed a large amount of pus in the urine. A urine culture now showed an atypical B. Coli. The hemoglobin was 72 per cent. An intravenous

FIG. 2. Same as previous showing the right half of the horseshoe by retrograde. On cystoscopy four ureteral openings were found.

urographic examination showed the excretion on both sides to be good, but revealed the presence of four conducting systems (Fig. 1): An apparently normal and fully developed right upper urinary tract (A); a normally rotated left upper pelvis which appears stunted (B), as seen in a double kidney; caudad to the above, there are two separate pelves, one on either side of the vertebral column, with their calyces pointing mesially, assuming the form of a horseshoe kidney (C & D). The left component (D) of the horseshoe as well as its ureter appears dilated in contradistinction to the

ureter leading from the overlying stunted left pelvis, while the right half
(C) of the horseshoe is seen displacing the upper ureter of the right upper
pelvis.   In other words, the left half of the horseshoe is seen to be the site
of the uretero-pyelonephritis.

A cystoscopy confirmed the presence of four kidney systems, four
ureteral orifices having been observed; both mesial ureteral orifices ap-
peared normal with good indigo-carmine excretion issuing from each.
The left lateral ureteral orifice conforming to the lower pelvis of the horse-
shoe (D) was patulous, and no indigo-carmine was observed to flow from

FIG. 3. Same as previous case to prove the presence of horseshoe kidney by
retrograde pyelogram, showing the left side.

it.   The right lateral orifice conforming to the right lower pelvis of the
horseshoe (C) appeared uninvolved and the indigo-carmine excretion was
fair.   The urine from the bladder contained many white blood cells; that
from the right lower pelvis (C) contained only a few red blood cells.   On a
second cystoscopy a fair indigo-carmine excretion from the left lower
pelvis (D) was obtained; the urine specimen was turbid and contained
many white blood cells.   Retrograde pyelograms (Figs. 2 and 3) of both
lower pelves corroborated the presence of the horseshoe component in a
case of quadruple kidney.

The child was placed on a ketogenic diet in an attempt to acidify the

urine to a point of a pH 5.6. With this, urotropine, ammonium chloride and sodium acid phosphate were administered. The urine, which at first contained from 15 to 20 white blood cells per high power field, was at one time reduced to 1 white blood cell per high power field. Just before leaving the hospital, the patient showed 2 or 3 white blood cells per high power field.

Summary. A rather rare congenital anomaly, that of a quadruple kidney with a horseshoe component is presented. Its recognition was aided by excretion urography. Incidentally, the value of the procedure, particularly in children, is stressed, and it is suggested that a diagnosis of simple "pyelitis" should only be made when all other pathological alterations in the urinary tract are excluded by a thorough urologic investigation.

MONOCYTOID MYELOBLASTIC LEUKEMIA

LOWELL A. ERF, M.D.

[From the Service of Dr. B. S. Oppenheimer and from the Laboratories]

During the past year, three cases of leukemia have been observed which, at first, were considered to be examples of mixed leukemia. Cells of both the myeloid and monocytic series seemed to be present. However, during the terminal stages of the process, more myeloid cells appeared, and at terminus, a typical myeloid leukemic blood picture was present. It is the purpose of this paper to offer a rational explanation of this apparent transformation. The case history that follows is a typical example.

History (Adm. 372090). A 31 year old Jewish salesman entered the hospital, complaining of weakness and fever. He had had a tuberculous hip during childhood; otherwise his past history was negative. His recent illness began ten weeks before admission, at which time several teeth were extracted with much bleeding. During the two weeks following extraction, the patient felt weak, but in the course of five weeks had regained good health and continued well for another three weeks. He then developed a very painful swelling of the left lower jaw. The dentist lanced the gum (under nitrous oxide anesthesia) in the region of the second lower left molar and obtained a small amount of pus. However, the swelling continued, and the patient began to have weakness, anorexia, sweating, and fever. The dentist referred the patient to a physician, who, suspecting leukemia, sent him to the hospital. The patient was admitted in a state of marked prostration.

Physical Examination. The patient appeared to be acutely ill, pale and with a perceptible pyrexia. There was a marked swelling on the right side of the face and a purpuric eruption on the chest and neck. The outer side of the right upper gum had a large slough, and the left lower, a small one. There was marked edema involving gums, palate and cheek. All of the lymph nodes were enlarged, especially the posterior cervicals. The liver extended 4 cm. below the costal margin, and the spleen was 2 cm. below the costal margin.

Hematological Findings. The white blood count varied from 50,000 to 100,000, with the hemoglobin maintaining itself at about 50 per cent during hospitalization. The platelet count remained within low normal limits. The differentials showed the polymorphonuclear neutrophiles to be between 15 and 25 per cent, myelocytes between 10 and 15 per cent, myeloblasts between 30 and 40 per cent, lymphocytes between 2 and 5 per cent,

and *monocytoid cells* varying between 20 and 30 per cent. A typical count follows: (October 15, 1934).

Hemoglobin.. 47 per cent
Red blood cells.. 3,450,000
White blood cells.. 79,000
Platelets... 130,000

Jenner-Giemsa	per cent	*Supra-Vital*	per cent
Non-Segmented Neutrophiles....	8	Polymorphonuclear Neutro-	
Segmented Neutrophiles.........	7	philes.......................	3
Myelocytes Neutrophilic........	14	Myelocytes A..................	4
		Myelocytes B..................	4
		Myelocytes C..................	15
Myeloblasts Neutrophilic........	42	Myeloblasts...................	41
Monocytoid Cells...............	22	*Monocytoid Cells*...............	28
Basophils.....................	1	Basophils.....................	1
Lymphocytes..................	6	Lymphocytes..................	4

Interpretation of Blood Findings. Were these primitive monocytoid cells, monocytes or myeloid cells? With Jenner-Giemsa stain, they varied between 15 and 25 micron in diameter, having an irregular outline or border, and exhibited a hazy, slightly granular, moderately blue-gray cytoplasm that contained a markedly irregular nucleus, the chromatin of which was in fine granular masses. The chromatin was not the uniform reticular type characteristic of the myeloblast nor the coarsely granular type of the lymphoblast. In some, the chromatin was arranged in a homogeneous smooth network. A few had nucleoli and some had vacuoles. Most of these cells had small granules that were faintly oxidase positive. Supravitally, these cells varied between 20 and 30 microns in diameter. Many had serrated margins. They exhibited a whitish, cloudy cytoplasm containing many small, irregularly dispersed vacuoles in association with a few small, indistinct granules and distinct rod-shaped mitochondria. The vacuoles did not enlarge uniformly in the neutral red supravital preparations as is characteristic of monocytes. The nuclei were bizarre in shape, and the chromatin was clumpy. The centrosome was distinct in some and absent in others. Most of these cells had very active motility, even more active than that of normal polymorphonuclear neutrophiles.

Course. The disease process was rapidly progressive. A constant temperature between 102°F. and 104°F. was maintained. Transfusions and Fowler's solution were given, but the patient died fifteen days after admission.

Necropsy Findings. An acute leukemic process was found involving

nearly all of the organs, especially the spleen, liver, lymph nodes, and bone marrow. There were petechial hemorrhages in the pericardium, pleura, mitral valve, and skin. Multiple infarcts of the spleen were present, and there was a parenchymatous degeneration of the liver. Healed apical tuberculosis was revealed, associated with a chronic tuberculous epididymitis, and a healed tuberculosis of the right hip.

The hyperplastic marrow had a dull grayish-pink color grossly, and microscopically the sections revealed many myelocytes and many cells similar to myelocytes without granules. These cells had pale staining, homogeneous cytoplasm with large, irregular nuclei whose chromatin was in small clumps. The peroxidase stain was positive only in a few of these cells. There was no hyperplasia of the reticulo-endothelial system.

COMMENT

To some extent, chronic leukemia can be differentiated clinically into two main groups: lymphatic or myeloid, depending on splenomegaly and lymphadenopathy. In acute leukemia this is almost impossible. Similar difficulties are encountered at post mortem, both grossly and histologically, especially in the acute cases which have the same fundamental pathology, that of infiltration. Monocytic leukemia with hyperplasia of the connective tissues (Doan (1)) is difficult to diagnose at post mortem. The classification of leukemia is, therefore, essentially a cytological or hematological problem, and the most accurate diagnosis can be made only when the variations of the blood cells are followed and associated with the clinical changes of the patient. Bone marrow studies are usually very helpful. Smears of the fresh living marrow cells, obtained by puncture or biopsy, are preferable.

The monocytoid cells under discussion are probably atypical myelocytes or myeloblasts. This opinion is based on sternal marrow studies, supravital studies of the cells in relation to motility, vacuolization and granulation, and on the clinical and hematological process.

It was after a study of many sternal bone marrow punctures that a rational diagnosis of these atypical monocytoid cells was possible. Many marrow cells were found that were identical with myelocytes with the exception of granules. Whether such cells had not matured sufficiently to have granules, is unknown. Possibly the marrow has only a limited reserve of material from which granules are made. Perhaps sudden demands for increased amounts of granular material cannot always be met by the body; or a certain amount of time may be required for its proper development. Perhaps the nucleus has multiplied and matured faster than the cytoplasm, as Arneth (2) has described. He defines them as cells with "precocious nuclei." It may be possible that granules form only in mature cytoplasm. In marrow puncture smears it is possible to see granules forming in one

pole or portion of the cell cytoplasm and gradually spread throughout all of the cytoplasm, much like bacteria would develop.

Supravitally the monocytoid cells were not monocytes for several reasons; for example, these cells had active motility, which is not characteristic for monocytes; and the vacuoles did not develop uniformly in the neutral red supravital preparations. Monocytic vacuoles will enlarge and reach a nearly uniform size in about three hours in such preparations (3). Vacuoles of other cells enlarge irregularly, if present. The mitochondria were more characteristic of the myeloid series than the monocytic series; i.e., the mitochondria were rod-shaped and not threadlike.

The supravital characteristics in general were more compatible with the myeloid series although the morphological similarity to monocytes was marked.

An occasional cell of the monocytoid type had Auer bodies which are definitely myeloid granulations, as proven by the oxidase reaction. Probably the small granulations were proneutrophilic or undeveloped neutrophilic granulations. Anagnostu (4) believes that azurophilic granules are of such a nature and mature into neutrophilic granules. He describes the monocytoid cells with characteristics of monocytes on one hand, such as the cytoplasm, the size and shape of the cell, the absence of the perinuclear light area, and the frequent absence of definite nucleoli, but with characteristics of myeloblasts on the other hand, such as the shape of the nucleus and the quite homogeneous chromatin of the nucleus, and also by the fact that the nucleus is not "bubbly" as in the monocyte.

Naegeli (5) considers these cells as myeloblasts for he feels that the monocytic and granular series have the same origin, and he reports several cases of leukemia that had a monocytic picture at first, which developed later into myeloblastic leukemia. Schilling (6) believes that there is a monocytic type of leukemia and a monocytoid myeloblastic type of leukemia.

It seems rational that these "monocytoid cells" are agranulocytic myeloid cells in which the nuclei have matured from the round myeloblastic state, but in which the cytoplasm had failed to accumulate granules.

CONCLUSIONS

1. A case report of an atypical myeloid leukemia is presented.

2. The cytology is discussed and an attempt is made to classify the atypical cells as improperly matured myeloid cells.

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HEMOPTYSIS AS THE PRESENTING SYMPTOM OF CONGENITAL CYST OF THE LUNG

JEROME L. KOHN, M.D.

[Service of Dr. Bela Schick]

The following case is an instance of a large solitary cyst of the lung in a child observed for a period of nine years. Her presenting symptom has been occasional hemoptysis. She was said to have had a pneumonia at one year and again at four years of age. It is during this second illness that she had her first hemoptysis. In the interval between these hemoptyses, the child has felt well, attended school, and presented no physical signs of pulmonary disease.

CASE REPORT

History (Adm. 286514). A female child, aged 7 years, was first admitted to the hospital on October 14, 1926. She was said to have had pneumonia at the age of one year and again when she was 4 years old. During this second illness she had an hemoptysis followed by cough of six months' duration. She was well until 5 days before this admission, when she had a second hemoptysis accompanied by a moderate rise in temperature and a slight cough. Examination of the lungs showed moderately impaired resonance at the base of the left lung, with diminished breath sounds over this area. A roentgenogram of the chest showed an annular shadow behind the left border of the heart on the level of the eighth rib posteriorly, interpreted as a cavity. During bronchoscopy, pus was seen exuding from both the upper and lower lobe bronchi of the left lung. For several months thereafter these bronchi were irrigated bronchoscopically.

The patient remained well for fourteen months until December 23, 1927, when there was another hemoptysis. The physical signs at this time were the same as at the previous admission. Bronchoscopy at this time showed blood exuding from the left lower lobe bronchus.

At repeated subsequent examinations, tuberculin tests were negative and the child appeared well and developed normally. There was no repetition of the hemoptysis for six and a half years, until May 9, 1934. At this time she was admitted to the Coney Island Hospital where the examination disclosed impaired resonance and almost absent breathing over the left lower lobe, and some râles at the base of the right lung. The heart was displaced to the left side. A few days later the breath sounds were more pronounced although still diminished as compared with the right side. A roentgenogram at this time showed diminished aeration of the

left lung and displacement of the mediastinum toward this side. During the period of observation here, the lung became more aerated. The temperature was somewhat elevated, the highest being 101.4°F. on the second day.

A few months later (September 6, 1934), a roentgenogram made at the Mount Sinai Hospital, showed the circular shadow in the left lower lobe noted at the first admission seven years previously (Fig. 1). She was readmitted to the Coney Island Hospital on October 29, 1934 because of an upper respiratory tract infection. Here the cavity was outlined by

FIG. 1. Roentgenogram of the chest of case 3, aged 15 years, taken on September 7, 1934. This child was first seen when 7 years old. The roentgenogram shows a circular shadow behind the left border of the heart on the level of the eighth rib posteriorly. This circular shadow was already present on her first admission to the hospital.

iodized oil injected into the left main bronchus. There was perhaps a slight dilatation of the bronchi in the region adjacent to the cavity. The child was in excellent physical condition.

<div style="text-align:center">COMMENT</div>

The regular annular shadow without any evidence of inflammation of the surrounding pulmonary tissue as found on roentgen examination, justifies the conclusion that we are dealing with an air cyst of the lung. It is impossible to decide definitely whether this cyst was acquired or of congenital origin. While it is true that the history of two attacks of pneu-

monia early in life, and the presence of cough for a period of six months before the cyst was recognized, indicates the possibility that the air cyst was the result of a suppurative bronchopneumonia, it is also possible that the cyst was present before these attacks of pneumonia and therefore congenital in origin.

The literature pertaining to cysts of the lung was fully reviewed by Koontz in 1925. He collected 108 cases of congenital cysts of the lung, 43 of the cases occurring in children. Since then there have been further reports by Eloeser (2), Wood (3), Scott and Waltz (4), and others. In none of these reported cases was hemoptysis the presenting symptom. In a recent comprehensive paper by Hennell (5), however, there appears a report of a case that is comparable to the one that is discussed here. In the case reported, a man 46 years of age suffered hemoptyses on six different occasions during a period of 26 years. On each occasion the cough and constitutional symptoms were minimal and there was complete recovery from symptoms. The roentgen films revealed the presence of a number of circular and oval cavities in the lower half of each lung. In this case there was no antecedent history of inflammatory disease of the lungs and there was no clinical or roentgen evidence of any inflammatory change in the pulmonary parenchyma.

Hennell states: "The size of a cyst and the changes which it may show from time to time depend on the character of the bronchial communication. The cyst will remain of the same size, or enlarge very slowly, if its bronchial communication is in the nature of a two way valve. It will rapidly increase in size, and the intracystic pressure will rise, even to the point of rupture, if the bronchial communication is of the check-valve variety. On the other hand, the cyst will collapse if its bronchial communication is shut off and its air content is gradually absorbed."

In our case, in spite of the failure of the iodized oil injected into the bronchi to enter the cyst, the presence of air within the cyst proves that a communication between the two really existed.

Hennell believes a pneumothorax, by producing pulmonary relaxation, may result in complete occlusion of the already imperfect communication between the bronchus and the cavity. This might lead to the obliteration of the cyst through the absorption of its air content, provided the source of continued renewal air through open bronchial communication is abolished.

Obliteration of the bronchial communication may possibly result from the irritation by the iodized oil injected into the bronchus or into the cyst itself, or may result in the closure of the cyst. In our case this did not occur following the single injection of iodized oil into the bronchus. The cyst may be obliterated by means of various operative procedures, but we considered these too hazardous to employ in a case such as this where the symptoms are few and the lesion does not constitute an impediment to the child's development. If, on the other hand, the hemoptyses should

become more frequent, or other complications ensue, operative treatment must be considered.

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SUDDEN PROFOUND ACROCYANOSIS AS THE PRESENTING SIGN IN MYOCARDIAL INFARCTION*

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AND SIMON DACK, M.D.

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Coronary thrombosis not uncommonly is ushered in by a state of shock with failure of the peripheral circulation. The patient is in collapse, perspiring freely and cyanotic. The blood pressure is low and the pulse rate is increased; the neck veins are collapsed. The skin of the extremities is cold and moist, and in the severer cases, marmorated. Such a picture, when accompanied by precordial pain, is readily recognized as resulting from coronary thrombosis. Great difficulty in diagnosis, however, was presented by a case without cardiac symptoms but with the circulation to the extremities almost completely cut off, causing symmetrical, blackish discoloration of the hands and feet. Necropsy disclosed widespread myomalacia of the left ventricle. We have found no previous report of such a condition.

History (Adm. 387561). A 59 year old ticket collector at a railroad station was first observed two years previously. At that time a pseudo-cyst of the pancreas was marsupialized. No abnormality of the cardio-vascular system was noted; the blood pressure was 118 systolic and 86 diastolic. Following the operation the patient was without symptoms until ten days prior to his admission, when he vomited black material and passed a tarry stool; this was repeated the day before coming to the hospital. At this time, the patient began to experience occasional precordial pain of moderate degree.

Physical Examination and Clinical Course. The patient was pale and slightly cyanotic but not dyspneic or orthopneic. The heart was not enlarged. The blood pressure was 80 systolic and 60 diastolic but soon fell to 65 systolic and 50 diastolic. The hemoglobin was 45 per cent. Following a transfusion it rose to 53 per cent. On the third day all the extremities suddenly became cold and cyanotic, the discoloration being sharply demarcated above the wrists and ankles. The pulses became imperceptible but later the radial returned, particularly on the right side. Immersion in warm water effected no change. There was edema of both

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* This case as well as the following one, with four other cases to appear in subsequent issues, constitute a group presented at the conferences of the Cardiovascular Division of the hospital.

legs. The veins of the lower limbs, particularly the femoral, and several veins in the upper extremities were thrombosed. Chemosis of the conjunctivae appeared. The heart sounds became very faint. The blood pressure remained at 90 systolic and 60 diastolic. An electrocardiogram showed marked abnormalities in the ventricular complexes indicative of severe myocardial damage. The patient did not rally and died two days later, the color of the extremities not having changed.

Necropsy revealed hemorrhage from a chronic duodenal ulcer, myomalacia of the anterior and posterior walls of the left ventricle and distal three-fourths of the interventricular septum; severe sclerosis of both main coronary arteries and the left anterior descending branch, but no actual thrombosis; acute passive congestion of the liver, pulmonary edema and right hydrothorax.
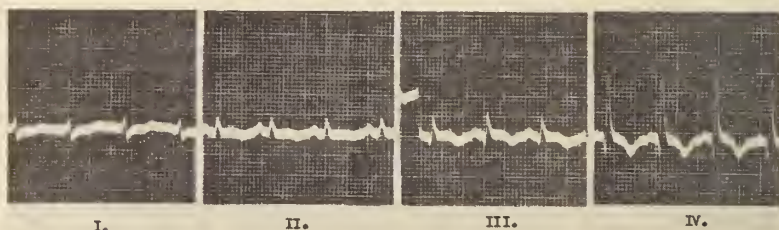
Electrocardiogram taken one day after collapse. Sinus tachycardia, rate 120 beats per minute, low voltage and slurring of the QRS, small Q-3 present. Abnormal RS-T transition intervals in Leads 1 and 3, T-1 small, T-2 and T-3 inverted. Precordial lead normal.

This illustration has been included by error in an article by the same authors in the March– April issue of the JOURNAL on page 289.

COMMENT

The diagnosis in this case was obscure. The intense cyanosis and coldness of the distal portions of the extremities, together with the disappearance of the peripheral arterial pulsations, suggested either multiple arterial embolization from an intramural or aortic thrombus, or a ball-valve thrombus obstructing the mitral or aortic openings. The presence of widespread peripheral venous thrombosis and edema of the lower extremities pointed to venous obstruction as a possible cause. However the consensus of opinion was that the clinical picture was due to severe peripheral circulatory failure due to shock resulting from either a recurrent pancreatitis or massive concealed hemorrhage. It was only when the electrocardiographic findings indicated severe involvement of the myocardium that the heart seemed the most likely cause of the peripheral circulatory failure despite the fact that there was little in the clinical course to indicate coronary thrombosis. This was proven at autopsy. Although no actual thrombosis was found in the coronary vessels, an acute myo-

cardial injury had occurred, for almost the entire left ventricle and inter-ventricular septum were the sites of myomalacia.

Although the early clinical picture of coronary thrombosis may be predominantly that of shock, such profound peripheral circulatory failure as was present in this case is uncommon. The mechanism of this syndrome is two-fold. When myocardial infarction occurs, the acute failure of the heart results in a marked diminution in cardiac output and circulatory blood volume. Simultaneously there is reflex dilatation of the peripheral capillaries (vasomotor paralysis); as a result, the peripheral venous pressure is reduced and the venous return to the heart and the cardiac output diminished. The prolonged bleeding from the gastro-intestinal tract further reduced the circulating blood volume and increased the shock. All these factors together were sufficient to bring the circulation in the distal parts of the extremities to almost a standstill and to result in the remarkable clinical syndrome described.

Conclusion. A case is presented of severe myomalacia of the left ventricle due to coronary artery disease in which the peripheral circulatory failure was so severe that it resulted in symmetrical blackish acrocyanosis.

ECTOPIC KIDNEY

Report of Two Cases

MORRIS A. GOLDBERGER, M.D.

[From the Gynecological Service of Dr. R. T. Frank]

The recognition of the true character of pelvic masses felt in the course of a gynecological examination is sometimes very difficult. This is particularly true when they are not related to the reproductive tract. An ectopic kidney should be suspected when a mass is felt at or below the brim of the pelvis, especially if it is more readily palpable by rectum.

The development of the kidney from the stage of pronephros and mesonephros to that of the metanephros is a rather rapid process. During this period the kidney, as the ureter increases in length, migrates upward and also rotates around its longitudinal axis. The close proximity of the kidney to the umbilical arteries and the bifurcation of the aorta may, at times, interfere with its migration and rotation and may cause its fixation in the pelvis as an ectopic kidney. Such congenitally misplaced kidneys are usually fixed and their ureters are short. Their blood supply usually comes off slightly anterior to the location of the misplaced organ and frequently close to the bifurcation of the aorta, or from the common or internal iliac arteries.

The ectopic kidney, if uninfected, gives no symptoms, but, in women, in whom the condition is more common than in men, may cause dyspareunia and occasionally may interfere with pregnancy and parturition.

Two instances of ectopic kidney were seen on the gynecological service in the course of one month.

CASE REPORTS

Case 1. History (Adm. 389046). The patient was a 55 year old woman, gravida 4, para 2. Amenorrhea had followed a pelvic operation nineteen years previously. A diagnosis of "congenital abnormality of the kidney" had been made at that operation. She was treated for pulmonary suppuration twelve years ago. She also had mild diabetes which was readily controlled by diet. The patient entered the hospital at this time because of vaginal protrusion for four years, associated with urinary frequency, dysuria, and incontinence on straining.

Examination. General: Blood pressure was 144 systolic, 70 diastolic. There was moderate peripheral sclerosis. The heart was slightly enlarged to the left. There was an occasional extrasystole. The lower pole of the right kidney was palpable.

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Pelvic examination. There was an egg-shaped cystocele, thin-walled, with tense mucosa over a midline scar. There was a moderate prolapse of the posterior vaginal wall, and an extremely short vaginal canal. The cervix was atrophic. Deep in the left pelvis, well below the sacral brim, a rounded mass could be felt.

Laboratory Data. Blood examination: Hemoglobin 80 per cent; sedimentation time, one hour; urea nitrogen 18 mgm.; sugar 290 mgm.; Wassermann negative. Urine examination: glycosuria 1.2 per cent; maximum concentration to 1.081. Intravenous pyelogram showed the presence of a left sacral kidney with a short ureter; the pelvis and calyces were not dilated; the right upper urinary tract appeared normal (Fig. 1). Electro-
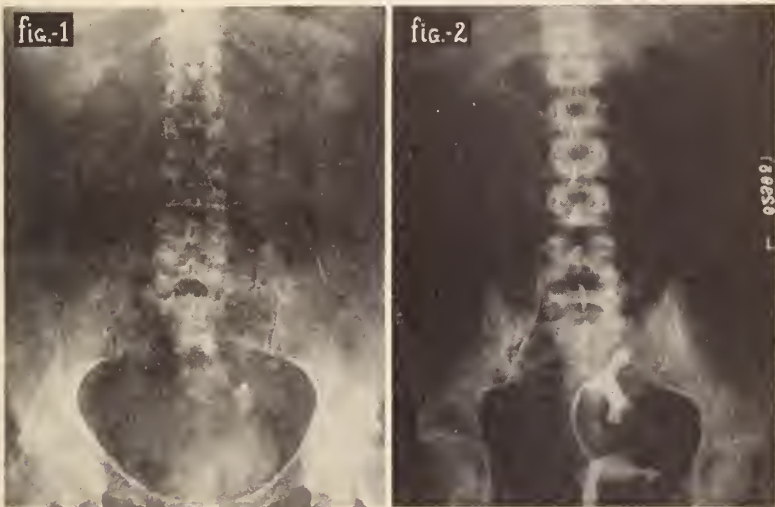

FIG. 1. Intravenous pyelogram showing left sacral kidney with a short ureter. The right kidney is in normal position.

FIG. 2. Retrograde pyelogram showing left sacral kidney with a short tortuous ureter. The right kidney is in normal position.

cardiogram showed sinus tachycardia, frequent ventricular premature contractions, left ventricular preponderance, suggesting hypertrophy of the left ventricle with involvement of the ventricular muscles.

Course. Under parasacral anesthesia a modified LeFort operation was performed. The patient's postoperative convalescence was uneventful and she was discharged twenty-seven days after operation. The final examination showed a short vagina approximately $\frac{3}{4}''$ long; the vaginal mucosa was healed; the anterior and posterior walls did not descend on pressure; there was no urinary incontinence.

Case 2. History (Adm. 389919). The patient was a 25 year old woman, nulligravida, with a normal menstrual cycle. Her past history included a

left salpingectomy seven months prior to admission for a supposed left ectopic tubal pregnancy. For four months following the operation pelvic diathermy treatment was given for a left pelvic inflammatory mass. She complained of slight introital dyspareunia since her marriage but now entered the hospital because of left lower quadrant pain of two weeks' duration.

Examination. Blood pressure was 145 systolic, 88 diastolic. Pelvic investigation revealed a normal, nulliparous introitus and a small cervix far back. The uterus which was of normal size was anteflexed, and ante-verted. Behind and to the left of it was a tense mass extending into the pouch of Douglas. The mass was partially fixed, the upper limit could not be defined fully, and it appeared to be intraligamentous.

Laboratory Data. Blood examination: Hemoglobin 100 per cent; sedimentation time one hour, 50 minutes; urea nitrogen, 15 mgm.; Wasserman, negative. Urine analysis negative. Cervical smear negative.

Course. In view of the patient's history of a recent operation followed by an inflammation of the left pelvis, it was considered likely that the mass arose from the left ovary. An exploratory laparotomy was performed under gas-oxygen-ether anesthesia on February 10, 1936. The uterus and right adnexae were found to be normal. The left tube was absent; the left ovary, which was found suspended from the lateral pelvic wall, appeared slightly enlarged, and contained a corpus hemorrhagicum. The mass which was felt on pelvic examination was found to be retroperitoneal. The peritoneum over it was incised for a distance of two inches, and one pole of the retroperitoneal mass was gently delivered through the opening. It was immediately apparent from the lobulated smooth contour and firm consistency that it was an ectopic sacral kidney. The kidney was immediately replaced, care being taken not to produce torsion of the pedicle. The posterior parietal incision was closed. Palpation of the left upper quadrant revealed no kidney in the left lumbar fossa, while the right kidney was felt in its normal position. The abdomen was closed without drainage except for a small subcutaneous rubber dam to drain a stitch abscess which was encountered under the old scar.

The patient's postoperative course was uneventful except for a transient albuminuria and microscopic hematuria. At the time of the patient's discharge, fourteen days after operation, the abdominal wound was well healed, the urine was clear, and the patient had no complaints. She returned one month later for an x-ray examination of the genito urinary tract following retrograde pyelogram (Fig. 2).

SUMMARY AND CONCLUSIONS

1. Two cases of ectopic kidney are reported.

2. In the first case the condition was established by intravenous pyelography.

3. In the second case the condition was discovered during an exploratory operation and the operative findings were later confirmed by retrograde pyelography.

4. The importance of intravenous pyelography is stressed in retroperitoneal pelvic tumors.

5. Ectopic kidney should be suspected when retroperitoneal masses are felt at or below the brim of the pelvis.

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PITUITARY TUMORS

Report of Two Cases with Pathological Findings Contrary to the Roentgenographic Interpretation

ABRAHAM KAPLAN, M.D.

[From the Neurosurgical Service of Dr. Ira Cohen and the Neurological Service of Dr. Israel Strauss]

In the attempt to collect all the preoperative evidence which aids the neurosurgeon in the precise localization of an intracranial tumor one can hardly afford to omit detailed roentgen studies of the skull.

Any method that will enable one to approximate a preoperative pathological diagnosis will be of inestimable value not only in the operative approach to the lesion, but also in the preparations and methods of attack in any given case. The neurosurgeon is vitally concerned with data which may help to reveal the nature of the growth. Many intracranial tumors are known to have a characteristic appearance, familiar modes of extension and points of attachments, all calling for selective methods of surgical attack. Similarly, certain types of these tumors often show roentgenographic changes which are so characteristic that we have come to accept them without hesitation.

Thus in the study of the two cases to be reported it was found that although the clinical manifestations were very similar, the x-ray abnormalities pointed very definitely in one patient to a craniopharyngioma, and in the other to an adenoma of the pituitary. That exactly the reverse was found at operation is of interest, and places us on guard not to lean too heavily upon what appears to be conclusive x-ray interpretation, as to the histology of the lesion.

CASE REPORTS

Case 1. History (Adm. 389604). A 40 year old storekeeper was admitted on February 5, 1936 because of intense frontal headaches. Since early childhood he had been suffering with nasal trouble, diagnosed as ozena. At the age of 23 he began to have nocturnal "asthmatic" attacks which continued for about 12 years and then disappeared following a nasal operation. Five years before admission, mild frontal headaches were first noted. These continued until one year ago when they became more severe, at times continuing for several hours. Coughing, sneezing, or straining would initiate and aggravate the headaches. At such times there was associated severe pain over the sacral region. Three weeks be-

fore entry, the headaches and pain over the sacrum became so intense that he was confined to bed for a week. Temporary diminution of vision in the left eye was first observed two years before admission. For a year there were spells of blurred vision while reading, or on walking from an illuminated room into a dark one. During the past two years memory for names and numbers had been faulty. At times he felt as if he were in a "fog." There were also episodes of vertigo, generalized weakness, and lassitude. For the past ten years there was a steady increase in weight, about twenty-five pounds. Sex life since early manhood had been inadequate. He remained single. Since the age of twenty, it was necessary for him to shave only once a week. Polydypsia averaging from 15 to 20 glasses of water a day was not unusual and at times he was awakened at night by thirst.
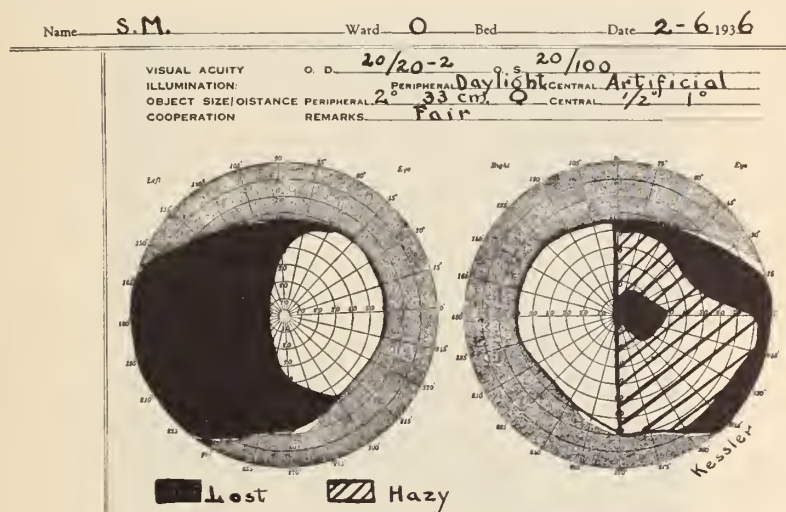

Fig. 1. Preoperative record of visual acuity and fields of vision

Examination. He was a moderately obese man with eunichoid habitus. The skin of the trunk was soft and white but the hands and feet had a cyanotic hue. The fingers were delicate and slightly tapering, and very little hair was found on the face, chest, or in the axillae. The pelvis and hair about the pubis were of the female type. From the right nostril there was a slight mucopurulent discharge and the left middle turbinate was absent. Blood pressure, systolic 120, diastolic 95. Pupils were equal, reacted promptly to light and in convergence. There was slight pallor of the left disc and some fullness of the retinal veins in the left fundus, but the fundus on the right failed to show the slightest abnormality. Visual acuity and fields were as charted in Fig. 1. There was a suggestive flattening of the right side of the face. There were no other abnormal neurological signs.

Laboratory Data. The urine only showed a slight trace of sugar. On three separate occasions the blood Wassermann was positive. Spinal fluid had an initial pressure of 80 mm., appeared pinkish yellow, and the supernatant fluid was xanthochromic. Pandy 1 plus, Wassermann negative. One week later studies of the spinal fluid showed an initial pressure of 70 mm.; it appeared uniformly pink, and again the supernatant fluid was xanthochromic. Basal metabolic rate, plus 22. Glucose tolerance test was as follows: Fasting 109.3 mg. per 100 c.c.; at $\frac{1}{2}$ hour 149.3 mg.; at 1 hour 196.1 mg.; at 2 hours 129 mg.

Roentgen films of the skull (Fig. 2) showed a marked enlargement of the sella turcica in the anterior-posterior diameter, partial erosion of the posterior clinoids, also irregular calcification in the suprasellar region extending across the midline but chiefly to the left.

Fig. 2. Enlarged Sella Turcica with suprasellar calcification

Course. Operation February 20, 1936, by Dr. A. Kaplan. Under avertin and local anesthesia, a right transfrontal craniotomy was performed. As the right frontal lobe was elevated there came into view the flattened right optic nerve accompanied by its vein. To the medial side of this structure a reddish brown tumor could be seen bulging upward at least one centimeter above the chiasm. The rounded mass was solid, did not pulsate, and was seen to cross the midline underneath the lower margin of the falx. The tumor wall was incised, and most of it was excavated with curette and suction. The left optic nerve was not visualized. Postoperative course was uneventful. Headaches disappeared promptly and visual acuity and fields taken 12 days later showed definite improvement (Fig. 3). The patient was given a course of x-ray therapy to the region of the sella

turcica.   In a recent check up, improvement in vision was noted also in the left eye.   Polydypsia had decreased from 15 to 20 glasses of water a day, to 8 glasses a day.

Microscopic Report (Dr. J. H. Globus).   The tissue is composed of columns and groups of cells surrounded by blood spaces showing abundant vascular channels, large areas of frank hemorrhage and a scant stroma. There are also large numbers of dark staining calcifications scattered throughout, apparently hyalinized and calcified walls of small vessels. The tumor cells are fairly uniform with rounded vesicular nuclei and dark staining chromatin granules.   Many of these nuclei possess a nucleolus. The cytoplasm is moderate in amount and stains diffusely blue.   Diagnosis: Chromophobe adenoma.
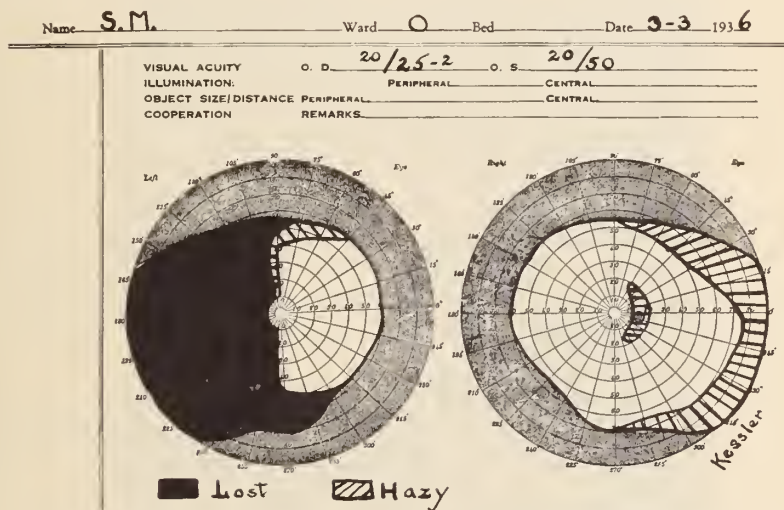

Fig. 3. Post-operative record of visual acuity and fields of vision

COMMENT

Perhaps one of the most surprising features of this case is the innocent appearance of the fundi in the presence of such a large neoplasm in the region of the chiasm.   There is a strong probability that the neoplasm had forced its way through the diaphragma sellae early in its growth, encroaching upon the olfactory nerves and in this way was responsible for the prolonged nasal trouble.

Calcification within a chromophobe adenoma is unusual.   Calcified shadows in the suprasellar region strongly favor the diagnosis of craniopharyngioma, for in about 80 per cent of these tumors x-ray will reveal such calcified markings.

In the face of positive evidence of an intracranial neoplasm, a positive blood Wassermann should not and did not delay operative intervention.

The xanthochromia in the spinal fluid may best be explained by the vascularity of the tumor which was in such close proximity to the subarachnoid space.

Case 2. History (Adm. 390012). A 44-year old laborer, admitted on February 17, 1936, complained of progressive decline of vision for five years. Married at twenty-six years, he has two living children and there were two miscarriages. Since early childhood he was troubled with "acute rhinitis" and in May 1915 a "cosmetic" nasal operation was performed. Diminution in vision in the left eye was first noted in 1931. Objects which first began to appear blurred, soon could be distinguished only as shadows. Gradually vision in the left eye declined so that one and one-half years later he was totally blind in that eye. During this period there were recurrent attacks of epistaxis, about two a month, and these were accompanied by mild frontal headaches. He was given treatments for ozena but these influenced neither the headaches nor the failing vision. For eight months he had sharp pains over the right temporal region, which as a rule were relieved by aspirin. At times, these attacks would last all day. Two months before admission vision in the right eye began to fail. Objects appeared hazy and frosted until the morning of December 22, 1935, when, as he was about to start off for work, he found himself totally blind. Since then the attacks of pain over the right temporal region completely disappeared. For about two years there was a steady diminution in libido. No unusual thirst or somnolence was noted but there was a loss of 15 pounds during the preceding six months.

Examination. He was a short, obese, middle-aged man, totally blind. There were no constitutional signs to suggest pituitary disturbance. Anosmia was complete on both sides. The teeth were in a very poor condition and there was the typical fetid odor characteristic of ozena. The moderate tremor of the hands and tongue was said to have been present for many years. Blood pressure: systolic 170, diastolic 110. Pupils were widely dilated, equal, and slightly irregular. There was only very slight reaction to very strong light which he was unable to perceive in either eye. Fundi showed primary optic atrophy more marked on the left. The vessels were thin but otherwise appeared natural. The left palpebral fissure was wider than the right. A few nystagmoid jerks were noted on extreme lateral gaze.

Laboratory Data. Urine was negative; red blood cells numbered 4,440,000; leucocytes 7,100 of which 69 per cent were neutrophiles and 23 per cent lymphocytes. Hemoglobin was 89 per cent. Blood Wassermann was negative. Spinal fluid showed a pressure of 130 mm. There were two monocytes, a negative Pandy test, a Total Protein of 40 mgm., and negative Wassermann and colloidal gold reactions.

X-ray of the skull (Fig. 4) showed marked destruction of the sella turcica and posterior clinoids. The dorsum sellae was completely de-

stroyed. The floor of the sella turcica was deeply depressed into the sphenoid sinus. There was also evidence suggestive of erosion of the left petrous apex. Posterior to the sella turcica there was also a suggestion of a calcified shadow.

Course. Operation February 27, 1936, by Dr. Ira Cohen. A right transfrontal craniotomy was performed under avertin and local anesthesia. The anterior horn of the right ventricle was tapped and 90 cc. of clear fluid was removed by aspiration. The entire frontal lobe collapsed and was then easily elevated. The right optic nerve readily came into view. It appeared rather pale and was seen to be tightly stretched over a rounded projecting mass. This greyish tumor did not pulsate and seemed to

Fig. 4. "Ballooned" Sella Turcica

elevate the entire chiasm putting such tension on the left optic nerve that it appeared elongated, flattened and almost white. The tense wall of the tumor was shiny and fluctuant. Aspiration yielded 20 cc. of greenish brown (motor oil) fluid. The cyst was incised, and the contents emptied, exposing a cavity which occupied the extent of the "Ballooned" sella turcica. Washings from the cyst showed cholesterin crystals. The cyst fluid contained 250 mg. per cent of cholesterol. A considerable portion of the adherent cyst wall was peeled away from the optic nerves and chiasm so that they were no longer compressed. The interior of the cyst was swabbed with Zenker's solution. Hemostasis was well controlled and the wound closed in layers.

Postoperative course was satisfactory. On several occasions there was a

rise in temperature with a corresponding fall in pulse rate. This disproportion suggested a disturbance in the regulatory mechanism of the tuber cinereum. At times, he was able to perceive a flickering light in the temporal field of the right eye. On other occasions, he recognized moving shadows before the right eye. On the whole it was rather disappointing to find so little restoration of vision.

Microscopic Report. (Dr. J. H. Globus). The specimen is composed of whorls of interlacing sheaves and wavy bands of thick collagenous fibers which in some portions have become acellular and partly hyalinized. Other portions show young, active fibroblastic cells. Numerous capillaries ramify throughout the tissue and there are numerous perivascular hemorrhages. The tissue is probably the wall of a cyst but there is no evidence of an endothelial lining. Diagnosis: Craniopharyngioma.

COMMENT

The x-ray films and the absence of constitutional signs made us suspect a pituitary adenoma rather than a congenital (Rathke pouch) cyst. Had the presence of primary optic atrophy, even on one side, suggested the taking of x-ray films at an earlier date, we might have saved sufficient vision to enable him to return to his usual occupation.

The experiences with cases similar to the two reported, seem again to emphasize that in the presence of mild headaches and progressive decline of vision one should not wait until optic atrophy is unmistakable but to resort to earlier and if necessary repeated studies of visual fields, and roentgen films of the skull.

CLINICAL PATHOLOGICAL CONFERENCES

GEORGE BAEHR, M.D., AND PAUL KLEMPERER, M.D., *presiding*

Wednesday, October 14, 1936

Case 1. Subacute Bacterial Endocarditis (Streptococcus Viridans) Following A Tooth Extraction. (From the Medical Service of Dr. B. S. Oppenheimer)

History (Adm. 395327). The patient was a 53 year old tailor. He began to experience some dyspnea on exertion one year preceding his admission to the hospital. Six weeks ago he had a tooth extracted. (This event should be noted in view of the subsequent events, for the extraction of teeth with apical infections may distribute bacteria into the blood stream.) Two weeks after the extraction he began to experience frontal headaches, chilly sensations and his temperature rose to 103°F. He also had sweats and a migrating "arthritis" involving successively the ankles, hips and small joints of the fingers. These joints became tender and swollen. He also experienced pain over the precordium which increased on deep respiration.

Examination. The patient was a pale, thin, middle-aged male. There was a leathery friction rub over the left anterior chest between the 6th and 8th ribs. Both bases posteriorly were dull and diminished breath sounds and fremitus were present. The heart was enlarged to the left and a loud rough systolic thrill was palpable and audible over the right second intercostal space. Over the aortic area a loud, rasping systolic bruit was present, while at the apex there was heard a loud, rough systolic murmur. There was also a pleuropericardial rub over that area. The rhythm was coupled as in pulsus bigeminus. There was no edema or cyanosis. The blood pressure was 90 systolic and 60 diastolic.

Laboratory data. The sedimentation rate was rapid—25 minutes. The hemoglobin was 71 per cent; the white blood cells, 12,400 with 70 per cent of polymorphonuclear neutrophiles. The urine was negative. An electrocardiogram revealed sinus tachycardia LVP, prominent P_2, RS-T transitions slightly elevated in all leads, T waves of low voltage. An X-ray examination of the chest revealed generalized enlargement of the heart; both left and right ventricles were enlarged. There was a small effusion at the left base.

Course. It was at first thought that this patient with aortic stenosis and mitral insufficiency was suffering from an acute attack of rheumatic fever. This diagnosis was based on the presence of fever, polyarthritis, pleuritis, pericarditis and pleuropericarditis in a patient with definite physical signs of a valvular lesion. The absence of a previous history of an acute rheumatic episode was noted at that time. But, due to the fact that cases with rheumatic valvular disease are seen occasionally without a definite previous history of rheumatic fever, this point was not considered as contradicting the diagnosis. The patient ran a febrile course, the temperature ranging between 101°F. and 103°F. A transient pericardial friction rub was heard the day after admission. Nine days after admission a pleural aspiration was done and 120 cc. of blood-tinged fluid was obtained. The fluid clotted after standing for 20 minutes. There were no organisms on culture. The pleural effusion in-

creased so that a Potain aspiration was done and 1050 cc. of fluid removed.   Edema of the ankles was noted and this was attributed to the presence of hypoproteinemia (total protein 3.9 per cent).   The reduction in blood protein was believed to be due to prolonged protein starvation.   Several transfusions were given.   Salicylates were administered.   The temperature returned to normal and remained so for two weeks, when he was discharged from the hospital.   It is to be noted that blood cultures were not taken during this period.

The patient remained well for two weeks after which he again began to complain of migratory joint pains, dyspnea and chilly sensations.   He was readmitted a month after discharge.   At this time two very important additional physical findings were noted: 1) the presence of a white centered petechia in the conjunctival sac; 2) a slight tendency to clubbing of the fingers.   Because of these observations, the diagnosis was made of a superimposed subacute bacterial endocarditis.   Important confirmatory laboratory data were: 1) progressive anemia (hemoglobin falling from 60 per cent to 40 per cent); 2 persistent albuminuria; and 3) microscopic hematuria.   The electrocardiograms taken this time showed a prolonged PR interval (.20) in addition to the changes described previously.   Blood cultures were taken on three occasions and all were reported negative.   No macrophages were found in the blood.   At no time was the spleen palpable.   Fever continued with elevations to 104°F.   The sudden onset of pain in the left lower chest was interpreted as due probably to splenic infarction.   An erythematous nodule (Osler node) appeared on the volar surface of the right index finger.   The ability to concentrate urine was present on admission but was lost later and the specific gravity became fixed at (1.010).   Toward the end the urea nitrogen mounted to 46 mgm. per 100 cc.   The possibility of a bacteria-free stage of subacute bacterial endocarditis was suggested for this reason and because of the persistently negative cultures.   The patient developed repeated attacks of paroxysmal tachycardia and died in one of these episodes, four months after the onset of his illness.   The last blood culture was reported positive for streptococcus viridans—one day after death.   This case was considered clinically as one of rheumatic chronic cardiovascular disease, aortic stenosis and mitral insufficiency with a recurrent attack of acute rheumatic fever at the age of 53 years, followed by a superimposed subacute bacterial endocarditis due to streptococcus viridans.

Necropsy Findings.   The pericardium was dull, thickened and covered by fibrinous material.   100 cc. of sanguinous fluid was found in the pericardial sac. The heart weighed 620 gm.   The left ventricle was markedly dilated and hypertrophied.   Upon opening the left ventricle, there was seen a markedly distorted aortic valve which was so stenotic that the lumen did not admit more than a thin probe.   It was further occluded by a large firm mass of vegetations.   The cusps were so distorted that they could not be distinguished.   The process had extended above the valve to the base of the aorta, the inner coat of which was destroyed in such a fashion as to form a large ulcerated excavation—a mycotic aneurysm.   The base of this cavity was formed by the fibrous tissue of the pericardium covering the outer wall of the left atrium.   It was obvious that the infection of the pericardium was by direct extension from this area.   The wall of the mycotic aneurysm was thin and devoid of elastic tissue.   Rupture would surely have resulted were it not for the presence of the extremely stenotic valve which reduced the pressure of the blood entering the aorta.

Comment by Dr. Klemperer. In view of the clinical picture during the first admission, it is important to determine the presence of a rheumatic process. One can draw no conclusions from the appearance of the aortic valve. We must, therefore, look at the other valves. The mitral valve is thin, delicate and shows no evidences of rheumatic involvement. The chordae insertions are thin and weblike. This is also true of the tricuspid valve. We must next look at the auricular endocardium for the presence of MacCallum's lesions. Again there appears to be no change, the endocardial surface shows no thickening and finally, upon careful microscopic study of the sections of the myocardium from various parts of the ventricles and auricles, no Aschoff bodies have been found. Only small embolic areas with inflammatory cell reaction are seen. We are, therefore, forced to say that there is no evidence of preëxistent rheumatic disease in this heart. The aortic valve might have been a bicuspid one, the seat of arteriosclerotic changes. The other organs show evidence of embolization. There are multiple infarcts of the kidney, with small hemorrhagic spots which microscopically are focal embolic lesions. The spleen shows a perisplenitis and an old healed infarct. The pleural cavities contained serosanguinous fluid and the surfaces were covered by shaggy fibrous adhesions. There have been repeated observations of aortitis in cases of subacute bacterial endocarditis but this one illustrated to an unusual degree the damage which may result from such a process. The pericarditis and the pleuritis were both due to direct extension of the infection through the wall of the aorta.

Comment by Dr. Baehr. It has often been said that "pericarditis is not a part of the picture of subacute bacterial endocarditis." This is not strictly true. Pericarditis may occur in this disease and, when it does, there are three possible explanations for its presence. First, there may be a coexisting acute rheumatic fever; pericarditis is a common feature of the latter disease, and several authors, including Pappenheimer and Von Glahn, have published observations upon the coexistence of the two diseases in a large percentage of their cases. Second, one third of the cases of subacute bacterial endocarditis in the bacteria free state are complicated by a glomerulonephritis, and a uremic pericarditis may occur under these circumstances. Third, pericarditis may be due to streptococcus infection itself. This is unusual, as Libman has emphasized, but it may occur, as this case illustrates, due to the penetration of a mycotic aneurysm into the pericardium and extension of the infecting organisms into the pericardial sac. I should like to stress the fact that the clinical picture of subacute bacterial endocarditis in this patient closely simulated acute rheumatic fever during the first admission. The case demonstrates the need for caution in diagnosing initial attacks of acute rheumatic fever in the middle-aged. The history of a tooth extraction preceding a febrile illness in a cardiac patient is of real clinical significance. One frequently finds streptococcus viridans in pure culture in apical tooth infections. Transient bacteremias with this organism may follow dental extraction. It is therefore not surprising that a history of a preceding tooth extraction is often obtained in patients with cases of subacute bacterial endocarditis. The possibility of subacute bacterial endocarditis should therefore be kept in mind when such a history is obtained in a patient with chronic valvular disease and persistent fever.

Reported by MORRIS STEINBERG, M.D.

Wednesday, November 11, 1936

*Case 1.   Acute Diffuse Pancreatitis Following An Alcoholic Debauch; Laënnec's
Cirrhosis (From the Medical Service of Dr. George Baehr)*

History (Adm. 398214).   The patient was a 68 year old woman who had been
an habitual drinker for over fifteen years.   Five years before admission she was
hospitalized for delirium tremens.   For the past three years she had been subject
to occasional nosebleeds.   About six days before entering the hospital, while in a
state of deep alcoholic intoxication, she began to complain of general weakness and
lassitude.   Epistaxis recurred more frequently.   Shortly before admission she
suddenly vomited considerable quantities of dark brown fluid.

Examination.   The patient was stuporous, moderately icteric, and vomited large
quantities of blood while being examined.   Her pupils were small, slightly irregu-
lar, but equal.   There were numerous large, dilated veins over the anterior chest,
shoulders and abdomen, forming a caput about the umbilicus.   The heart was
somewhat enlarged to the left and a harsh systolic murmur was heard over the
precordium.   The abdomen was soft and markedly distended.   A very large,
hard, irregular, freely movable mass, which was distinct from the liver above it was
felt.   A softer and smoother mass was felt to the left of the umbilicus.   There was
flatness in the flanks with a distinct fluid wave.

Laboratory Findings.   The blood pressure was 120 systolic and 50 diastolic.
The blood count disclosed 64 per cent hemoglobin, 2,810,000 red blood cells per
cu. mm. and 19,800 white blood cells per cu. mm. of which 88 per cent were poly-
morphonuclear leucocytes.   The blood chemistry findings were: urea 125 mgm.
per cent; sugar, 205 mgm. per cent cholesterol, 125 mgm. per cent with only a
trace of cholesterol esters.   The icteric index was 12, indicating the presence of 2.5
mgm. of bilirubin per 100 cc. of blood plasma.   The urine contained urobilin in a
dilution of 1 in 40.

Course.   The patient remained in deep stupor and died on the third day in the
hospital.   Her temperature ranged between 99 and 101°F. and just before death
rose to 104.6°F.   It was thought that death was due to hemorrhages into the gastro-
intestinal tract from varices secondary to Laënnec's cirrhosis of the liver (alcoholic).

Necropsy Findings.   The *abdominal cavity* contained about 600 cc. of thin sero-
sanguineous fluid.   The omentum and mesentery were studded with opaque
whitish yellow elevated areas of fat necrosis.   Within the omentum there were felt
indurated masses, some the size of a small grapefruit.   The *liver* had an irregular,
nodular surface.   Its edge presented three fingers below the costal margin.   Its
cut surface showed the finely granular appearance of cirrhosis.   The *spleen* was
enlarged and soft.   The *pancreas* was markedly enlarged and hard with its free
and cut surface studded with opaque white and yellow plaques of necrosis.   From
the center of some of these areas a thick, gelatinous, pus-like slough could be ex-
pressed.   The pancreatic duct was patent.   The *splenic vein*, at the point where it
receives the pancreatic branch, contained an adherent grayish thrombus.   The
kidneys displayed diffusely distributed ecchymoses on their surfaces.   The renal
glomeruli on microscopic examination were found to contain blood.   The *esophagus*,
in its lower end, at a point 2.5 cm. above the cardia, presented a small 2 mm. in
diameter ulceration in the mucosa.   A thrombosed vein seen directly above this,
was found to descend and traverse the ulceration.   A ruptured varix at the point
of ulceration had apparently been the origin of the profuse hematemesis.

Comment. Dr. Baehr stated that, with the predominance of symptoms referable to cirrhosis of the liver, and to severe alcoholic intoxication, the diagnosis of pancreatitis and fat necrosis could not be made.   There is a possibility that hemorrhages into the stomach, duodenum, and other viscera may have been due to the intense vomiting and retching which followed the last alcoholic debauch.   These hemorrhages into the wall of the duodenum, between the duodenum and pancreas and into the pancreas itself may have precipitated the terminal acute pancreatitis with fat necrosis.

Dr. Klemperer commented on the unusual finding of ecchymoses in the kidney. They were attributed to vascular damage, possibly due to resorption of pancreatic ferment.

<div align="right">Reported by Frederick King, M.D.</div>

Case 2.   Endemic Typhus Fever (Brill's Disease) (From the Medical Service of Dr. George Baehr)

History (Adm. 391466).   The patient, a 61 year old Jewish white male, entered the hospital with a three day history of moderately severe frontal headache, malaise, fever of 103°–104°F., and a slight cough productive of a small amount of mucoid sputum.   There were no ocular disturbances, vertigo, vomiting, or sore throat.   His previous history was essentially negative except for typhus fever in 1896, at the age of 21 years.   Pediculosis and the presence of rats in his residence were disclaimed.

Examination.   The patient was a well developed, well nourished white male, appearing acutely ill.   There was no sinus tenderness.   The conjunctivae and pharynx were deeply injected.   There was slight nuchal rigidity.   The chest showed diminished mobility of the thoracic cage and inspiratory retraction of the intercostal spaces.   Inspiratory and expiratory wheezes were present throughout both lungs.   Numerous fine crackling râles were found at the right base, a few similar râles at the left base and left inferior axilla.   The heart sounds were distant; there were no murmurs.   The rhythm was regular with an apical gallop.   The abdomen was soft but slightly distended.   The tip of the spleen was just palpable. The prostate gland was markedly but symmetrically enlarged.   The extremities, except for the presence of moderate sclerosis of the peripheral vessels, were negative. The skin everywhere, except that over the face, was the seat of innumerable pinhead to small pea-sized dark red to purplish-red macular papules.   The temperature was 104.4°F., the pulse 84, the respirations 18.   The blood count showed 8,750 white blood cells of which 88 per cent were polymorphonuclear leucocytes, 10 per cent lymphocytes and 2 per cent monocytes.   The hemoglobin was 98 per cent. The blood Wassermann test was negative, the blood urea, 23 mgm. and glucose 100 mgm. per 100 cc.   Urinalysis revealed a slight albuminuria.

Course.   The diagnosis entertained on admission was Brill's disease (endemic typhus fever) complicated by bronchopneumonia of the right lower lobe and chronic bronchitis and emphysema.   The Widal, para Widal, Felix-Weil agglutination reactions and blood cultures were negative.   The temperature continued between 103 and 105.3°F. during the first four days of hospitalization, while during the last three days it fluctuated between 100° and 105°F.   The pulse varied between 90 and 160 per minute.   Soon after admission the patient became very drowsy, apathetic; the skin eruption, aside from spreading to the forehead, re-

mained unchanged. The chest signs persisted. Three days following his admission nuchal rigidity became more marked and bilateral Kernig signs appeared. The cerebrospinal fluid obtained at this time was clear, colorless, showed an initial pressure of 70 mm. of water and contained 3 monocytes per cu. mm. The patient's apathy and torpor deepened; signs of bronchopneumonia persisted. The pulse became very rapid and thready. The patient succumbed to his illness one week after admission, on the eleventh day of his disease. According to the patient's history, he is reported to have been ill for only three days before admission and yet on admission the characteristic exanthem was present. The rash appears on the fifth day of the disease, rarely on the evening of the fourth day, so that we can assume that the patient was ill for a day or two longer than his history states and that he died of the cerebral and toxic manifestations of the disease on the 12th or 13th day after the onset, the days on which the critical drop in temperature occurs in most patients.

Necropsy Findings. The gross autopsy findings included a patchy bronchopneumonia confined to the right upper and lower lobes of the lung with pulmonary congestion, a moderate degree of fatty myocardial change and slight hypertrophy and dilatation of the right ventricle. Petechial hemorrhages were found in the skin, cortical surfaces of the kidneys and intestinal mucosa. Marked fibroadenomatous hyperplasia of the prostate associated with a chronic cystitis were also found. The *histopathological studies* revealed in various organs lesions of a specific character (Fig. 1). A section of skin removed for biopsy revealed a *necrotizing arteriolitis*, considered to be a vascular skin lesion originally described by Fraenkel as pathognomonic of typhus fever. The smaller vascular bed, including venules and arterioles, presented thrombosing and partially necrotic mural lesions and occasional endothelial proliferations. The thrombi were "hyalin-like" in nature and the affected portion of the vessel wall was surrounded by collections of small lymphocytes, plasma cells, histiocytic cells, and occasional polymorphonuclear leucocytes. Secondary to these vascular lesions there were foci of necrobiosis within the spleen with reticulum and plasma cell proliferation; degenerative, interstitial and focal pericardial inflammatory cell accumulations within the heart and degeneration and necrosis of renal parenchyma and striated muscle. The gross impression of extensive bronchopneumonia was confirmed in histologic preparations.

Comment. Dr. Baehr, pointing to the clinical differences between Brill's disease and epidemic typhus fever (Old World) and emphasized their seasonal differences. As Dr. Nathan E. Brill reported, this type of the disease occurs throughout the year with a tendency to an increased incidence in summer, whereas the epidemic form appears in the winter months of January, February and March. Nevertheless, the cross immunity experiments of Anderson and Goldberger and the more recent observation of Zinsser and Castanada and of the United States Public Health Service (Dyer, Rucker, Maxey, etc.) on the tunica vaginalis lesions in guinea pigs demonstrated that Brill's disease is Old World typhus, in contrast with the endemic disease in the southern states, which is New World typhus.

In regard to the mode of transmission, Dr. Baehr pointed out that the United States Public Health Service workers have demonstrated that the vector in New World typhus is the rat flea. The constant reservoir of the disease is infected rats and the disease is transmitted occasionally to humans by the rat flea. Although

Old World typhus is transmitted from man to man by the body louse, this does not seem to be the insect vector in Brill's disease. Nor can the rat flea be indicted. In fact, the mode of infection in Brill's disease is still a mystery upon which the
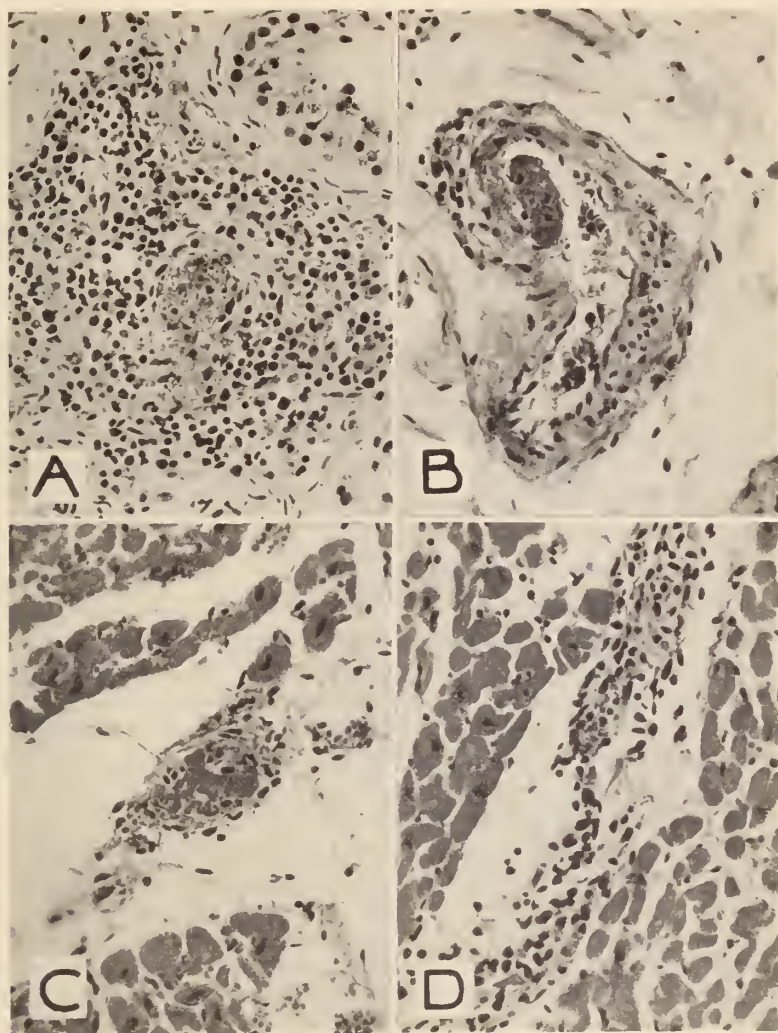

FIG. 1. Lesions in typhus fever: A. Necrotic arteriole in the testicle showing marked inflammatory cell infiltration with thrombosis. B. Arteriole of the testicle showing endothelial necrosis with thrombosis and perivascular cell infiltration. C. Necrotic arteriole with thrombosis within the myocardium. D. Myocardial cell infiltration.

recent work of Dr. Hans Zinsser, Professor of Bacteriology at Harvard, throws a new light. He observed that all the patients at the Massachusetts General Hospital with Brill's disease were Russian Jews who had come from Russia or central

Europe many years before. At Dr. Zinsser's request, a study was made by Dr. Frederick King of the clinical records of about 550 instances of Brill's disease in New York City, 341 of which had been hospitalized at The Mount Sinai Hospital. Dr. King noted that more than 97 per cent of the patients were Jews who had immigrated from Russia or Central Europe, usually 10 to 30 years ago. On the basis of these findings, Zinsser has proposed the hypothesis that the patients had originally been infected in Central Europe and that the disease had remained latent in them only to become reactivated under certain still unknown conditions many years after migration to the United States.

The low mortality of Brill's disease as compared to that of Old World typhus fever was stressed. Brill reported three deaths among 300 cases, in elderly enfeebled persons. During the last few years we have observed three more deaths. One private case, which Dr. Baehr had seen in consultation was in a man of 35, able-bodied and strong, who died of the cerebral manifestations of the disease with increasing nuchal rigidity and progressive stupor.

Reference was made to Rocky Mountain spotted fever, another Rickettsia disease which resembles typhus fever and is transmitted by a tick. Attention was called to the fact that several cases of Rocky Mountain spotted fever had been observed on Long Island during the past year. One must, therefore, assume that there is a reservoir of this disease among rodents on Long Island and that a tick is prevalent on the Island which can transmit the disease to humans.

<div align="right">Reported by HENRY HORN, M.D.</div>

Case 3. Massive Fatal Hematemesis From Gastric Ulcer In A Case Of Chronic Myeloid Leukemia (From the Medical Service of Dr. B. S. Oppenheimer)

History (Adm. 398951). The patient was a 54 year old Porto-Rican housewife who developed generalized aches and pains, anorexia and increasing weakness ten weeks before admission to the hospital. On the day before and during the day of admission she suffered several profuse hematemeses. She lapsed into coma just before entering the hospital. Since childhood she had had a swelling of the right leg, a finding present in other members of her family.

Examination. On admission the patient was comatose, had marked hyperpnea and appeared to be profoundly anemic. Her temperature was 101.2°F. Fundi showed a moderate number of new and old flame-shaped hemorrhages. The heart was not enlarged. Its sounds were of poor quality and the rate was 132. The blood pressure was 105 systolic and 65 diastolic. A hard spleen extended ten fingers' breadth below the costal margin, while the soft edge of the liver was palpable just below the right costal margin. There were extremely hard, bean-sized nodes in both inguinal regions. The skin of the right leg between the knee and the ankle was loose and thickened.

Laboratory data. The hemoglobin was 25 per cent. There were 535,000 white blood cells per cu. mm. with 17 per cent of segmented polymorphonuclear leucocytes, 20 per cent of the non-segmented form, 43 per cent of neutrophilic myelocytes, 7 per cent of myeloblasts, 6 per cent of eosinophilic myelocytes and 7 per cent of basophilic myelocytes.

Course. A half hour after admission the patient had another profuse hematemesis and, despite active treatment, went into shock and died within a few minutes.

In view of the patient's nativity, the greatly enlarged, hard spleen, and the

hematemesis, the first impression was bilharziasis (schistosomiasis) with cirrhosis of the liver and hemorrhage from ruptured esophageal varices. However, the blood picture was unmistakably that of myeloid leukemia. The swelling of the right leg was considered to be probably filarial.

Necropsy Findings. The *spleen* filled the whole left side of the abdominal cavity and weighed 3,000 grams. Its normal architecture was obliterated by the diffuse hyperplasia of the pulp and the infiltration with myelocytes and myeloblasts. The surface showed multiple infarcts. The *liver* was enlarged and had a mottled grayish brown color, and showed on cut section, small gray areas of infiltration. The *bone marrow* appeared gray and soft. The retroperitoneal, perigastric, peripancreatic and inguinal *lymph nodes* were enlarged. In the *stomach*, along the "magenstrasse" there were found several acute ulcerations, with one of these ulcers being the seat of bleeding and the cause of hematemesis.

Comment. Dr. Klemperer pointed out that the spleen, liver and bone marrow showed lesions characteristic of chronic myeloid leukemia. The gastric ulcers, he thought, were simple acute ulcers, not caused by infiltration of myeloid cells but probably a consequence of disturbance in circulation due to abnormal filling of vessels with white cells and, possibly, thrombosis.

Dr. Baehr remarked that this case served as another illustration of the fact that instances of chronic leukemia often go undiscovered for prolonged periods, sometimes for many years, and the patients succumb to other intercurrent diseases. In patients with chronic forms of leukemia, it is advisable, therefore, to consider the possibility that an independent, intercurrent illness may be the cause of the patient's symptoms.

The large hematemesis in the absence of a bleeding tendency in this patient should have aroused suspicion of the existence of a gastric ulcer or neoplasm. Bleeding from the gastro-intestinal tract does not occur in chronic, or even in acute forms of leukemia except as part of a constitutional bleeding tendency. Massive hemorrhages from the gastro-intestinal tract in patients with leukemia are due, as a rule, to local lesions in these organs, which are entirely unrelated to the constitutional hemorrhagic diathesis characteristic of this disease.

Reported by FREDERICK KING, M.D.

Wednesday, November 18, 1936

Case 1. Thrombosis Of The Portal Vein Due To Invasion Of Its Wall From Carcinoma Of The Gall Bladder Which Simulated The Clinical Picture Of Laënnec's Cirrhosis Of The Liver (From the Medical Service of Dr. George Baehr)

History (Adm. 394764). The patient was a 66 year old white male who had for many years indulged excessively in the use of alcohol. Three months before entering the hospital he first noticed swelling of the ankles and distension of the abdomen. The latter caused him considerable discomfort and he was unable to eat. During the six months preceding his admission to the hospital, his symptoms persisted and he lost 44 pounds.

Examination. The patient appeared chronically ill; he was thin and showed huge abdominal distention due to ascites. There was marked dullness and diminished breath sounds at the right base posteriorly and in the axilla. At the extreme

left base there was flatness with diminished breath and voice sounds. The heart was normal. The blood pressure was 120 systolic and 80 diastolic.

Laboratory Findings. The urine was normal. The blood count was normal. The blood chemistry findings were as follows: urea, 10 mgm. per cent; sugar, 85 mgm. per cent; cholesterol, 190 mgm. per cent with only a trace of cholesterol ester; icteric index 5; direct Van den Bergh negative, indirect 1:300,000, indicating the presence of 0.3 mgm. per cent of bilirubin; total protein 4.5 per cent of which 2.2 per cent was albumin and 2.3 per cent globulin.

Course. A paracentesis abdominis was performed and 9 liters of straw-colored fluid were removed. The ascitic fluid contained 480 cells per cu.mm., most of which were lymphocytes, and none appeared to be tumor cells. The diagnosis of cirrhosis of the liver with severe portal stasis was considered. He was given frequent intravenous injections of glucose without effect. The ascites rapidly reaccumulated after paracentesis. At the end of the first two weeks in the hospital he became stuporous, declined rapidly and died one week later.

The terminal stupor was ascribed to liver insufficiency (cholemia). The low blood cholesterol ester seemed to support this view. The hypoproteinemia was thought to be due to the loss of blood protein into the ascites.

Necropsy Findings. The *abdominal cavity* contained about 6 liters of turbid, sanguineous fluid. The liver edge was at the right costal margin. In the region of the gall bladder there were dense, fibrous, band-like adhesions to the hepatic flexure and to the transverse colon and duodenum. The *spleen* was totally ensheathed in a dense mass of adhesions which involved the diaphragm, the left lobe of the liver, the splenic flexure and the abdominal parietes. The *liver* was slightly smaller than usual and its cut surface showed the normal lobular architecture contradicting the clinical impression of cirrhosis. The *gall bladder*, which was buried in adhesions, was markedly thickened, somewhat larger than average in size and whitish in color. It contained mucoid fluid and three yellow stones. The latter were from olive pit to olive in size and had papillated surfaces resembling that of a mulberry. The region of the cystic duct was covered with dense, firm, white tissue which entirely surrounded the duct. The *cystic duct* itself was thickened, white and almost entirely closed. The surrounding firm tissue compressed also the *common hepatic duct*, narrowing it to about one half of its usual diameter. The *portal vein* was markedly thickened and was surrounded by a whitish, dense tissue. The intima of this vein was dull and grayish white. Adherent to the inner wall of its right main branch and, less extensively, along the left main branch, there was a friable, grayish red, rough, dull thrombus which partly occluded the lumen. This thrombus extended backwards along the entire *splenic vein* and almost completely occluded it. The *superior mesenteric* vein was similarly involved. There was an area of hemorrhagic infarction of the *jejunum* due to acute thrombosis of ramifications of the superior mesenteric vein.

Histological study revealed a scirrhous carcinoma at the neck of the gall bladder. The tumor had invaded the portal vein, and this accounted for the secondary organizing thrombosis of the portal, splenic and superior mesenteric veins. Chronic cholangitis and pericholangitis was also demonstrated. In addition, there were found confluent bronchopneumonia of the right lung and the lower lobe of the left lung, parietal thrombosis of the main pulmonary arteries and congestion and edema of the small intestine.

Comment. Dr. Baehr remarked that there was no clinical evidence on which the diagnosis of malignancy of the gall bladder could have been made. The rapid reaccumulation of ascites after paracentesis might have led to the suspicion of the presence of thrombosis of the portal vein or of widespread peritoneal metastases. However, the clinical picture of portal stasis, the abnormal liver function tests, the laboratory findings of subclinical icterus and the history of chronic alcoholism fully justified the diagnosis of cirrhosis of the liver.

Dr. Klemperer pointed out that the absence of widespread metastases to the liver was probably due to the limiting effect of the dense connective tissue surrounding the area immediately above the primary tumor.

Reported by FREDERICK KING, M.D.

CLINICAL NEUROPATHOLOGICAL CONFERENCE

Monday, December 14, 1936*

Israel Strauss, M.D., and Joseph H. Globus, M.D., *presiding*

Case 6.   Metastatic Adenocarcinoma of the Right Frontal Lobe.
Dr. Mark Gerstle, Jr.

History (Adm. 378632).   A 58 year old white man was admitted to the hospital on April 11, 1935, complaining of bulimia and polydipsia for three months.   For two weeks his memory had been impaired.   Eleven days prior to admission he became dizzy, fell and struck his head.   He did not lose consciousness but immediately afterward he noticed that his left arm was weak and that the right side of his head was painful.   The next day he had an attack of epistaxis.   On the day of admission he had urinary incontinence.

Examination.   The objective findings of significance were as follows: There was tenderness to percussion on the right side of the skull.   The patient walked with a shuffling gait, dragging the left leg more than the right.   The pupils reacted sluggishly.   There was bilateral papilledema.   There was a hemiparesis on the left side of the body including the face.   Hyperreflexia and the Babinski sign were present on that side.   The patient also exhibited mental changes characterized by poor memory and emotional instability.   A lumbar puncture yielded clear fluid under pressure of 230 mm. of water.   The fluid contained 6 cells and 95 mgm. of total protein per cent.   X-ray examination of the chest showed no evidence of tumor growth.

Course.   A diagnosis of a right frontal neoplasm was made and the possibility of its being metastatic in character was considered.   Since no primary focus was discovered an exploratory craniotomy was performed on April 18th, 1935.   A softened area was found in the right frontal lobe.   No definite tumor mass could be removed for histological study.   Following the operation the patient reacted poorly and he died three days later.

Gross Anatomy.   About the mid-portion of the right middle frontal gyrus was a defect measuring about 1½ cm. in diameter, surrounded at the periphery by soft, disorganized brain tissue (Fig. 10A).   Digital exploration showed that this defect communicated with a cavity which extended anteriorly almost to the frontal pole, ventrally almost to the base of the temporal lobe, and a short distance posteriorly. The brain substance surrounding this cavity was soft and disorganized but there was an area of moderately firm consistency posterior to the precentral gyrus.   In the depth of the longitudinal fissure, the anterior portion of the left gyrus cinguli, just overlying the corpus callosum, was a dark purplish, elevated area which bulged into the longitudinal fissure.   This was much firmer in consistency than the sur-

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* The first five cases of the conference appeared in the March-April issue of this Journal, Volume III, Number 6.

rounding brain tissue and was well circumscribed. There were a few atheromatous plaques in the vertebral vessels but none were found to be occluded. The pituitary body was normal.

Microscopic Anatomy. In a portion of the meninges subjacent to the nodule to be described, there was an increase in round cells and in cells containing pigment. One area (probably near the operative site) showed extravasation of red blood cells
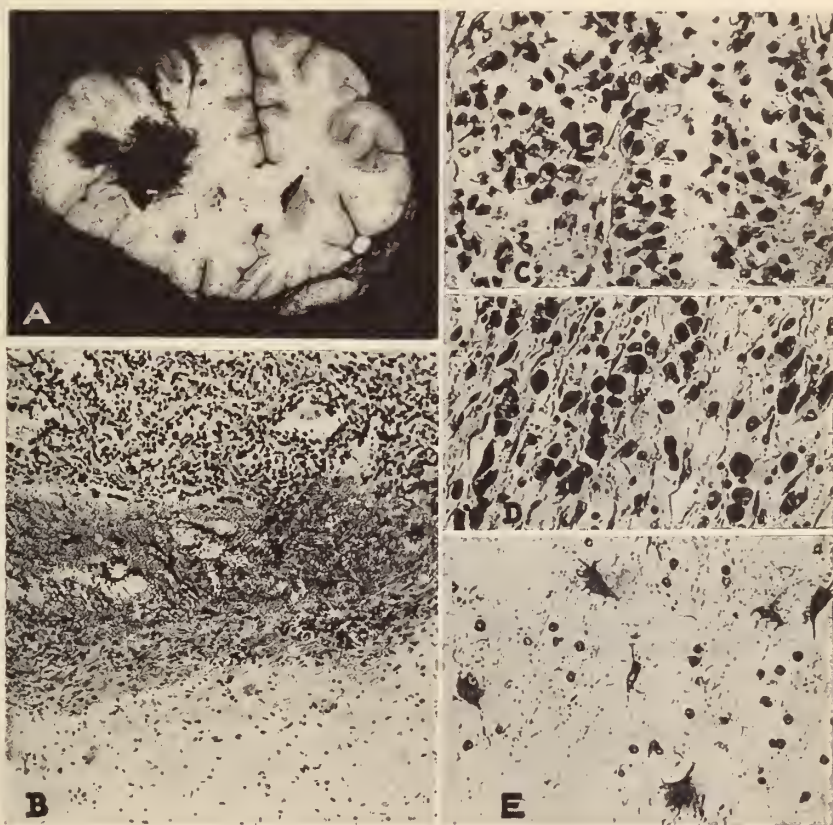

Fig. 10 (Case 6). A. Photograph showing tumor in the right frontal lobe. B. Section of the tumor showing cells arranged in irregularly branching acini (Hematoxylin and eosin stain). C. Tumor cells under higher magnification. D. Section of the tumor showing cells in the pigmented layer (Hematoxylin and eosin stain). E. Section of the tissue surrounding tumor, showing many ameboid glia cells (Hematoxylin and eosin stain).

and leucocytes in the leptomeninges. Sections of a tumor nodule showed it to be composed of cells arranged in irregular, branching acini (Fig. 10B, 10C). These cells varied in size and displayed an occasional mitotic figure. Surrounding the cellular area of the tumor there was a wide hemorrhagic zone, which in turn was surrounded by a layer of pigment containing cells (Fig. 10D). The tissue beyond this was disorganized and edematous. There were numerous amoeboid glia cells

(Fig. 10E) and almost complete falling out of nerve cells. One section passed through the chorioid plexus in which were found numerous psammoma bodies.

Comment by Dr. Globus. The histological appearance of the tumor is that of one mesodermal in derivation, probably primary in the perirenal region. Its cell arrangement, cell forms and the hemorrhagic character, justify its inclusion among the Grawitz type of neoplasm. The pigment was found to contain iron, hence it may be safely regarded as having its origin in laked blood. The malignancy of the lesion was, of course, indicated by the sudden onset and the rapid clinical course. Its expanding nature was pointed to by the papilledema. It was difficult to establish clinically its metastatic character without a detectable primary lesion. The numerous calcified bodies seen in the chorioid plexus is not a very rare finding. Their presence is readily explained by the fact that the chorioid plexus, being derived from the pia, is a very vascular membrane. The latter in its early formation presents an overabundance of blood vessels many of which remain unused and do not establish connections with patent blood vessels. Hence, they form blind loops and undergo degeneration. Thus, many of them in the course of degeneration undergo calcification and psammoma body formation, as seen in this case.

Case 7. Metastatic Carcinoma of Both Occipital Lobes.   Dr. Mark Gerstle, Jr.

History. (Adm. 375852). A 52 year old white woman was admitted for the first time on October 21, 1934, complaining of headache, which began three months previously. The important points in her past history included: (1) severe constipation and attacks of abdominal pain occurring several times a week; (2) frequent passage of blood per rectum, assumed to be due to hemorrhoids which she had had for five years; (3) periodic attacks of dyspnea for two years. Two months prior to admission the patient complained of noises in her head and flashes of light before her eyes. Simultaneously she noticed formication. Apathy, mental retardation and failure to recognize her daughter occurred on two occasions. The day before her entrance into the hospital her headache became intolerable, causing insomnia and resulting in a stupor, from which, however, she could be aroused. On admission she vomited bright red blood.

Examination. She was drowsy and disoriented. There was a left homonymous hemianopsia; bilateral papilledema and retinal hemorrhages more marked in the left eye. There was generalized hyperreflexia, more pronounced on the right side. The left arm was paretic. There was also a left sided astereognosis and slight hypalgesia of the right arm. The abdominal reflexes were absent. A Babinski, Gordon and Chaddock sign was present on the left side. X-ray examination of the skull showed almost complete absorption of the posterior clinoid processes with moderate absorption of the anterior clinoid processes. There were a few faint shadows in the right side of the skull just above the sella turcica, but it was uncertain whether or not they were within the calvarium. X-ray studies of the gastrointestinal tract revealed no evidence of a new growth in the stomach but there was a slight herniation of this viscus through the diaphragm. Several constrictions of the sigmoid were seen but thought to have been spastic in origin. The chest roentgenograms revealed no abnormal findings. The hemoglobin, on admission, was 74 percent and rapidly decreased to 50 percent. The spinal fluid was under a pressure of 140 mm. of water, contained twelve mononuclear cells, and albumin 4 plus. A craniotomy was performed on November 11th, 1934 and a

small, hard, well defined mass of the right occipital pole was enucleated. A specimen was reported to be that of a metastatic carcinoma. The postoperative course was satisfactory and two weeks later the patient was discharged much improved.

Readmission. She remained well for about one month, at the end of which time she began to show intellectual alteration, often became confused and disoriented. Her speech became thick and incoherent. She became incontinent of both urine and feces. She was then readmitted to the hospital on January 20th, 1935.

Examination. The abdomen was enormously distended with fluid. A hard, globular mass was felt in the rectum. She was restless and did not cooperate. There was motor and sensory aphasia. She was completely blind, the left pupil reacted sluggishly to light and was larger than the right. The face was drawn to the left and there was a bilateral Babinski sign.
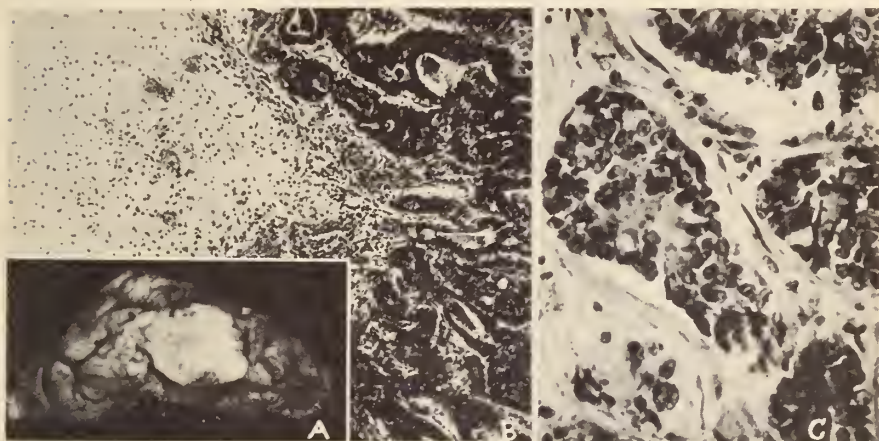
Fig. 11 (Case 7). A. Photograph showing tumor nodule in the right occipital pole. B. Section of the tumor showing invasion of the brain by tumor cells arranged in acini (Hematoxylin and eosin stain). C. Tumor cells under higher magnification. (Hematoxylin and eosin stain).

Course. Her temperature remained normal except on several occasions when it rose to 102°F. She would now and then emerge from her stupor but on the whole the course was progressively downhill, terminating in death on March 2nd, 1935.

Gross Anatomy. At the right occipital pole there was a small (3 by 2 cm.) hard, gray, lobulated nodule attached firmly to the dura, calvarium and to the subjacent brain tissue. On sectioning of the brain, a tumor mass was found at the tip of the right occipital lobe, apparently part of the tumor which was partially removed at operation (Fig. 11A). Another small tumor mass was found in the left occipital lobe. It measured about ½ cm. in its longest diameter. It was similarly hard and pearly gray in color.

Microscopic Anatomy. Sections stained with hematoxylin and eosin revealed masses of adenocarcinomatous tissue. These consisted of an acinous-like arrangement of the tumor cell separated by a fairly abundant fibrous tissue stroma (Fig.

11B). Under high power there were, in several acini, cells which were large and possessed an eccentric nucleus and clear cytoplasm. These appeared to be cells of the goblet type (Fig. 11C). In one place the neoplastic process had invaded the dura mater.

Comment by Dr. Globus. The histological appearance of the tumor is highly suggestive of its primary site being in the intestinal tract; the goblet cells and acinal arrangement favoring this view. This undoubtedly is so since the post mortem examination revealed a carcinoma of the sigmoid. It is not the first instance in which a metastatic tumor has been enucleated to give the patient a short respite.

Comment by Dr. Strauss. It is to be noted in this case that while the neurologic service diagnosed an intracerebral neoplasm, it was suspected that this neoplasm was of a metastatic nature. Everything was done that could possibly have been done to reveal a primary growth, but such a search was unsuccessful. We were therefore compelled to operate because of the possibility of the growth being primary in nature.

Occasionally with the full knowledge that a neoplasm is metastatic an operation is done in order to relieve the patient from the suffering incident to increased intracranial pressure. Such operation is frequently greatly beneficial to the patient not merely for the purpose of prolonging life but for the purpose of relieving the patient of intractable suffering.

Case 8.   Acoustic Neurinoma.   Dr. Jerome E. Alderman

History (Adm. 385763). A 51 year old man was admitted to the hospital on October 19, 1935. Since 1931 he had been complaining of throbbing headaches, most intense at the vertex. At times he would feel weak in the right lower extremity and the entire limb would twitch. These twitchings had increased in frequency, so that shortly before admission they would occur daily. Since 1932, he was subject to recurrent attacks of transient dimness of vision. For two years prior to admission there had developed tinnitus and impaired hearing on the right side. During the last three months there had been occasional morning vomiting.

Examination. The pupils were irregular and reacted sluggishly to light. They were unequal, the right being larger than the left. There was bilateral papill-edema. Both visual fields showed marked enlargement of the blind spots. There was bilateral deafness of the nerve type, more marked on the right side, with impaired vestibular responses on the same side. There was a right lower central facial paresis. The tongue protruded slightly to the right. The right knee jerk was more active than the left and the right abdominal reflexes were absent. An equivocal plantar response was elicited on the right side. A mental status disclosed no defects in memory, judgment or insight. The cerebrospinal fluid was under somewhat increased pressure (180 mm. of water) and contained 145 mgm. per cent of total protein. Roentgenograms of the skull were normal.

Course. The consensus of opinion was that the patient had an organic lesion in the left cerebral hemisphere affecting probably, the frontal or pre-frontal area. The character of the lesion was not identified and although its neoplastic nature was suspected, syphilis of the nervous system, lead encephalopathy or some pachymeningeal process were also considered. Since the laboratory studies of the blood and spinal fluid excluded lead, syphilis and any other inflammatory

disease, the diagnosis of neoplastic process was accepted. The clinical manifestations were interpreted as pointing to a supratentorial location of the lesion, since no cerebellar signs were noted. But, in order to establish the location with greater precision, an encephalography was carried out on October 25th. No air, however, entered the ventricular system, and only some of it was found in the subarachnoid space. Immediately following the encephalography the patient complained of headache but showed no other untoward results during the next four days until October 29th. The fact that air did not enter the ventricular system raised the suspicion of the likelihood of a posterior fossa tumor and caloric tests were requested. They were carried out by Dr. Maybaum who, in summing up his findings, said "There is bilateral hearing impairment of the nerve type greater on the right than on the left side. There is unequal spontaneous nystagmus directed to the right and left; it is finer and somewhat more rapid to the right, coarser and slower to the left. There is no spontaneous past-pointing. Caloric stimulation revealed diminished and delayed nystagmus on stimulation of the canals. Past-pointing is absent on stimulating the right horizontal and vertical canals. There is no vertigo." He followed this note by the following statement: "I am inclined to believe that we are dealing with a posterior fossa lesion. The tests show a preponderance of abnormal findings on the right side—for both cochlear and vestibular branches. It is possible that we are dealing with an angle neoplasm which has not completely destroyed the function of the right VIII nerve. I am impressed with the fact that this patient had little or no vertigo on stimulation of any of the canals, which favors a posterior fossa localization. It is possible that the bilateral hearing impairment may be an entirely independent factor— i.e. a purely peripheral involvement of the cochlear nerve (neuritis). The other findings, the absence of vertigo and past-pointing, speak for a localization in the posterior fossa."

A note on the chart on October 31, read as follows: "The patient is drowsy for the last two days. No discernible difference in reflexes." Since then he was apparently free of ill effects of the encephalography until November 2nd, when the patient was found to be somnolent but after being aroused appeared to be rational, alert and explained his somnolence by his inability to sleep at night. The papilledema was found to have increased; there was no evidence of meningeal irritation. The nystagmus on looking to the extreme right was marked and more intense than on the day of admission. Otherwise the findings were as heretofore. An opinion was given that the preponderance of evidence pointed to a supratentorial lesion rather than infratentorial. A few hours after this examination, on November 2nd, at 10:55 A.M. the patient suddenly stopped breathing, became cyanotic and flaccid. Artificial respiration and stimulation were applied at once. The pulse remained good all the time. He was placed in a respirator. The right lateral ventricle was then punctured, 80 c.c. of cerebrospinal fluid were removed and 25 c.c. of physiologic saline were injected by the endolumbar route in the belief that it would push upward a supposedly herniated medulla oblongata, but without effect; the patient ceased shortly thereafter.

Gross Anatomy. In the right pontocerebellar angle there was found a greenish brown tumor mass, the size of a plum (Fig. 12A). It was soft and adherent to the adjacent leptomeninges. It was situated along the right border of the posterior two-thirds of the pons and the upper one-third of the medulla oblongata.

A portion of the cerebellum which was adjacent to the tumor was markedly softened; the pons was flattened dorsoventrally and deformed. Numerous small branches of the basilar artery could be traced over the tumor.
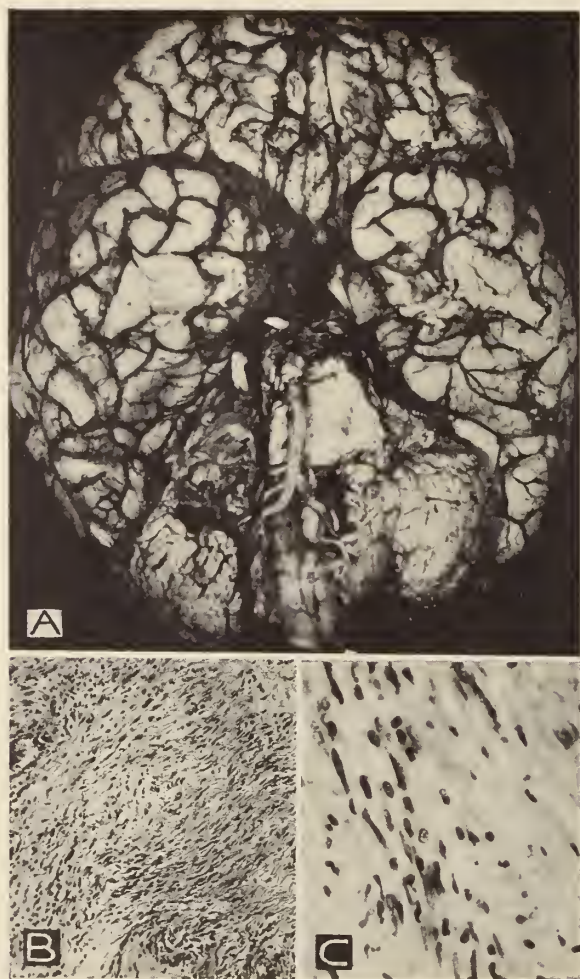

FIG. 12 (Case 8). A. Photograph showing the tumor in right pontocerebellar angle and the distortion of the pons. B. A section of the tumor (Acoustic Neurinoma) showing interlacing bands of tumor cells (Hematoxylin and eosin stain). C. Tumor cells under higher magnification (Hematoxylin and eosin stain).

Microscopic Anatomy. The tumor possessed a definite histological pattern. Bands of elongated cells formed interlacing tracts encircling areas in which the cells had a reticulum-like structure (Fig. 12B; 12C). Whorl formation was seen in some locations. Numerous large blood channels resembling sinuses were distributed throughout the field. Silver stains demonstrated tufts and brushes of nerve fibers. The elongated cells are of the type known as Schwamm cells which

form the neurilemmal sheath of nerve fibers. Thus, an appropriate name for this tumor would be Schwammoma. The term peripheral nerve glioma is also often used since these Schwamm cells are a variety of glial cells.

Comment by Dr. Globus. This case illustrates the difficulties that occasionally arise in the diagnosis of posterior fossa tumors, which not uncommonly simulate supratentorial tumors with prefrontal location. It also demonstrates the need of thorough and complete clinical study before encephalography is employed. On reviewing the various diagnostic steps in the study of this case, it will be noted that encephalography was undertaken before caloric tests had been done. The failure to carry out the caloric tests earlier in the study was very likely due to the fact that great, if not to say too great, weight had been placed on the signs and symptoms, such as the twitchings in the right limb followed by weakness and the the slightly increased deep reflexes and absent abdominal reflexes on the right side, which pointed to a left cerebral localization. Were the caloric tests carried out prior to the encephalographic study and had their diagnostic significance been accepted, then it is probable that no encephalography would have been undertaken and, if air injections were still considered desirable, the ventriculographic method of air studies would have been found to be the method of choice as less hazardous in suspected posterior fossa lesions. When now, the results of the caloric studies are added to the failure to get air into the ventricles by the endolumbar route, it becomes obvious that a posterior fossa tumor should have been more seriously considered. In view of the fact that the right vestibular system was more implicated than the left, the lesion could have been placed in the right pontine angle. Thus, in retrospect, it seems that a diagnosis of an angle tumor could have been made and that in view of the type of the tumor, there was promise of surgical relief.

Comment by Dr. Strauss. This case presented a very unusual and difficult problem in diagnosis. Ordinarily the diagnosis of a tumor of the acoustic nerve is one of the simplest in neurological practice. The history is a characteristic one, generally covering a number of years from the onset of the first symptoms to the time of operation. The symptoms began with tinnitus and a gradually increasing deafness. Later on, as the tumor grows the symptoms of intracranial pressure make their appearance as well as involvement of the cerebellum, pons and adjacent cranial nerves, such as the facial and trigeminal.

The symptoms referable to the acoustic nerve are also extremely definite. There is complete nerve deafness and generally complete absence of vestibular response. Likewise there is interference with the vestibular response of the opposite acoustic nerve though no impairment of hearing.

The case presented, however, began in 1931 with severe headache and at times a feeling of weakness in the right limb, also twitching of this limb. The twitching occurred very frequently and persisted up to the time of admission. There were likewise transient attacks of dimness of vision, very likely due to papilledema. At the same time there began to appear tinnitus and impaired hearing in the right ear.

The examination of the patient gave definite evidences of involvement of the right pyramidal tract, substantiating thereby the history of twitchings in the right leg and the hypothesis that the neoplasm was a supratentorial one somewhere in the

left cerebral hemisphere.   To make the diagnosis still more difficult it was found that the patient had bilateral deafness of the nerve type, with impaired vestibular responses on the right side, where the deafness was more marked.   The cerebrospinal fluid pressure indicated increased intracranial pressure.   Through an oversight on the part of the staff the caloric reactions were not taken when the general physical examinations were made, but only after an encephalogram had been done.   At no time were there any symptoms referable to affection of the cerebellum or the pons, despite the fact that autopsy showed a very marked involvement of both these structures.   After the encephalogram, the caloric test was made by Dr. Maybaum who found, as had the staff, a bilateral hearing impairment of the nerve type greater on the right than the left side; also the vestibular pathways on both sides were still active although there was diminished response to caloric stimulation on the right side.   The outstanding finding of this examination was that past-pointing was absent on stimulating the right horizontal-vertical canal, and there was no vertigo.   This led to the opinion that there was a posterior fossa lesion, and since there was a preponderance of the abnormal findings on the right side for both cochlear and vestibular branches, though present on both sides, he advanced the hypothesis that an angle neoplasm was present which had not completely destroyed function of the right 8th nerve.   However, after showing that he was cognizant of the unusual character of these findings in an acoustic nerve tumor, he suggested the possibility that the bilateral hearing impairment may be "an entirely independent factor, that is, a purely peripheral involvement of the cochlear nerve (neuritis)".

The patient's mental condition varied.   At some times he was wide awake and alert; at other times he was extremely drowsy.

Laboratory examinations of the blood and spinal fluid were made.   Lead, syphilis and any other inflammatory disease were excluded, the diagnosis of neoplasm being the one accepted by the staff.

On account of the history, physical findings and the inability of the staff to localize the neoplasm an encephalogram was done on October 25th.   The ventricular system was not outlined, which is not an unusual happening even in cases where tumors are supratentorial or where other disease conditions exist and it was then four days later that the caloric tests were made by Dr. Maybaum.

On November 2nd, 8 days later, the patient suddenly ceased breathing.   Because of the suspicion at this time that after all we were dealing with an infratentorial lesion, the right lateral ventricle was punctured.   80 c.c. cerebrospinal fluid were removed, with the idea of possible herniation into the foramen magnum; 25 c.c. of physiologic saline were injected by the endolumbar route with no success.

If the staff had not been led astray by the history of intracranial pressure, of involvement of weakness in the right leg and twitchings in that leg, by the incomplete involvement of the right acoustic nerve and the deafness in the left side, symptoms, as I stated, which are most atypical of acoustic neuroma, encephalography would not have been performed but recourse would have been had to ventriculography and the finding of a bilateral internal hydrocephalus would have made the localization definite, despite the contradictory nature of the symptoms as given in the history and the physical findings, with absence of cerebellar symptoms.

Case 9.   Schminke Tumor (Lympho-Epithelioma) With Invasion of the Base of the Brain.   Dr. John Scharf

History. (Adm. 378904).   A 34 year old man was admitted to the hospital on April 19, 1935.   Seven months before admission he began to be disturbed by colored lights but this was relieved by the wearing of smoked glasses.   Shortly afterward he began to complain of double vision, followed two months later by recurrent right frontal headache and pain in the right eye and right side of the nose.   Both eyes became swollen and discolored.   Three weeks later he began to experience constant pain and numbness in the region of the forehead and a dull ache on the right side of the face.   During the course of the illness he lost 30
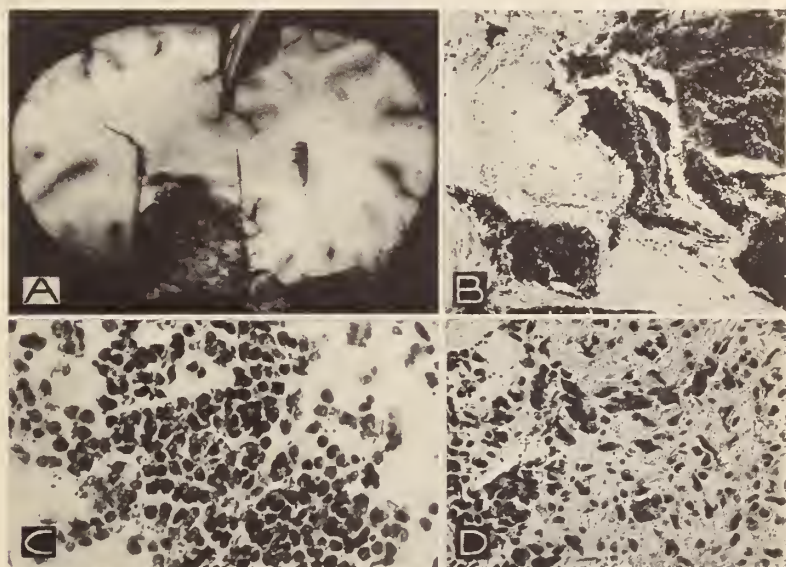
FIG. 13 (Case 9).   A. Photograph showing the tumor at the ventral aspect of the frontal lobes.   B. Dura mater invaded by tumor cells (Hematoxylin and eosin stain). C. Tumor cells (Lympho-epithelioma) under higher magnification (Hematoxylin and eosin stain).   D. Tumor cells invading cerebral cortex (Hematoxylin and eosin stain).

pounds in weight.   Sinus trouble was suspected and intensive deep x-ray therapy was administered to both antra and ethmoid sinuses.

Examination.   Both eyeballs were proptosed and there was marked restriction of the movements of the eyes.   The eyelids, forehead and scalp were markedly swollen and chemotic, the swelling extending backward to the occipital region. There was atrophy of the left optic nerve with consequent blindness in that eye. There was bilateral papilledema.   Vision in the right eye was diminished.   Aside from some mental retardation there were no other neurological findings.

Laboratory Data.   The cerebrospinal fluid was under a pressure of 300 mm. of water; it dropped to 70 mm. of water after removal of 20 c.c. of fluid.   X-ray studies of the skull showed marked destruction of the nasal and the adjacent frontal por-

tions of both orbits, with some involvement of the bridge of the nose and the left sphenoid bone. There were some dense shadows behind the sella turcica which appeared to be situated in the tentorium. The outline of the sella turcica was normal.

Course. A tumor, either intrasellar or suprasellar in location, was suspected and an exploratory craniotomy was performed. An extensive osteomyelitis of the frontal bone with some involvement of the dura mater was found. Large portions of the diseased frontal bone and granulation tissue were removed. The tissue was reported to be that of a lympho-epithelioma.

Following the operation, pus exuded from the wound. Two weeks afterwards there developed massive edema about both eyes, proptosis and immobility of the eyeballs, complete anosmia and total blindness. The pupils were large, irregular and fixed to light. Further radiation was contra-indicated as he already had received the full skin tolerance. He gradually declined and died on May 17, 1935.

Gross Anatomy. The post-mortem was limited to examination of the skull. There was extensive destruction of the frontal bone and of the base of the skull as far back as the anterior clinoid processes. The dura at the frontal poles was embedded in a mass of yellowish, soft, structureless tissue which also invaded the under-aspect of the frontal lobes (Fig. 13A). The floor of the anterior fossa was completely replaced by a similar tissue, in which numerous hard nodules could be felt.

Microscopic Anatomy. The dura was thickened and hyalinized and was invaded by massive nests of cells in irregular clumps and rosettes (Fig. 13B). For the most part they contained densely staining, large, round or ovoid nuclei with a narrow rim of cytoplasm. Other cells, especially those which formed rosettes, tended to assume a cuboidal form and contained more cytoplasm and a paler staining vesicular nucleus (Fig. 13C). Mitotic figures and amitotic division were frequently encountered.

A section of the cortex showed invasion by tumor cells, (Fig. 13D). In the subcortex there was an increase of glia. In that part beneath the tumor tissue the architecture was disorganized, the tissue being infiltrated by macrophages.

Comment by Dr. Globus. This is an unusual type of Schminke tumor. It shows not only the disruption and dislodgment of the cerebral tissue but its invasion by the tumor cells, a rather rare finding. The origin of the tumor, of course, is in some compartment of the nasal accessory sinuses.

Comment by Dr. Cohen. When I first saw this case this offered an unusual clinical picture. I thought it was osteomyelitis of the frontal bone and cavernous sinus thrombosis. However, when the microscopic report returned, it showed a Schminke type of tumor.

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Case 10.   Metastatic Melanoblastoma of the Left Occipital Lobe.
Dr. M. M. Kessler

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History. (Adm. 384888). A 25 year old male, was admitted to the hospital on September 25, 1935. Seven weeks earlier a growth, the nature of which is unknown, was removed from his forehead. Four weeks later he suddenly developed intense vertigo, nausea, and headache. The headaches gradually increased in severity and were localized to the left frontotemporal region.

Examination. The patient was disoriented and coöperated poorly. His tem-

perature at the time of admission was 97.4°F. There was tenderness to percussion over the left side of the skull. The right palpebral fissure was wider than the left. The pupils were irregular in shape and were almost fixed to light. There was impaired lateral gaze in both horizontal directions and nystagmus on lateral

Fig. 14 (Case 10). A. Photograph showing tumor in left parieto-occipital lobe. B. Collar arrangement of tumor cells about blood vessels (Hematoxylin and eosin stain). C. Tumor cells containing pigment (Hematoxylin and eosin stain).

fixation. The left fundus showed papilledema with hemorrhages and exudates and the right showed a nasal elevation of the optic disc. There was a right homonymous hemianopsia. There was a right central facial weakness. The deep reflexes were depressed but equal in the upper extremities. They were active in the lower extremities with the left knee jerk more so than the right. There was

a bilateral Babinski sign. Anomia and a sensory aphasia were present. The neck was moderately stiff and the Kernig sign was present on both sides.

Course. The blood hemoglobin was 110 per cent. A lumbar puncture yielded xanthochromic cerebrospinal fluid under an initial pressure of 260 mm. of water. Its protein content was 80 mgm. per cent. The Wasserman test on the bood was negative. X-ray examination of the skull was also negative.

A lesion in the left cerebral hemisphere was diagnosed. Because of the advancing stupor, an exploratory operation was performed. A needle was passed into the substance of the brain. A gush of dark blood, which continued to well up in large amounts, resulted and blocked further manipulations. The next morning the patient's condition became worse and he ceased later in the day.

Gross Anatomy. The entire left occipital lobe was soft, fluctuant, and larger than its fellow. Nearly the entire left occipital lobe and part of the posterior half of the left temporal lobe were occupied by a large brownish, brittle mass. This mass had the appearance of a hemorrhage, yet was much more cohesive than ordinary blood clot and contained within its center a small island of whitish tissue. (Fig. 14A.)

Microscopic Anatomy. Sections of the tumor showed cells forming collars many rows deep around the small blood vessels (Fig. 14B). The cells were small, round or polyhedral, with scanty cytoplasm and small round vesicular nuclei. Many of the cells contained coarse brown pigment granules (Fig. 14C). These cells were scattered diffusely throughout all parts of the tumor. Some of the cells had become fragmented and their pigment granules were strewn among the interstices of the tissue. The pigment was shown not to be ferruginous in origin by subjecting the tissues to a special stain for iron. The "dopa" staining method was then applied, which showed the presence of melanin granules in some of the cells. Many mitotic figures were present. Large areas of hemorrhage were scattered throughout the tumor. The adjacent brain showed a marked increase in glial nuclei and severe degenerative changes in the ganglion cells.

Comment by Dr. Globus. The tumor displayed the characteristic features of metastatic melanomata involving the brain. They include the small size and polyhedral form of the cells, the scanty amounts of the melanin pigment and its distribution in the stroma of the tumor as free coarse granules or as a pigment dust. These features serve to some extent as points of differentiation between the metastatic tumors and the primary melanoblastic lesions of the nervous sytem.

The case ran a rather unusual clinical course since the symptoms referable to the nervous system came on so rapidly and soon after the removal of some skin lesion.

Case 11.   Large Tuberculomata of the Brain.   Dr. David Beres

History. (Adm. 371694). A 50 year old colored man was admitted to the hospital for the second time on October 3, 1934. At the age of 25 he was supposed to have had a chancre, which was treated only locally. In August, 1929 he had been struck on the back of the head by a lead pipe, was unconscious for half an hour and suffered from headache for six days afterward. Two years later, in September, 1931, he suddenly found himself unable to formulate words to express thoughts which were entirely clear in his mind. The episode lasted for about five minutes and then recurred two or three times a month, gaining in severity. Eight months later twitching of the lower part of the right side of the face was followed by

twitching of the whole face and closure of the right eyelid. Beginning with September, 1932 there appeared attacks of convulsive seizures affecting the right arm, which were followed by long periods of aphasia. A report from another hospital where the patient was investigated in February, 1933, showed that the Kahn test performed on the cerebrospinal fluid and blood was negative. The colloidal gold curve was meningitic in type. An encephalogram gave evidence of retraction of the right hemisphere and the presence of adhesions in the left fronto-parietal region. In March, 1933 he entered the hospital for the first time.

Examination. The right palpebral fissure was wider than the left. The pupils were equal but reacted sluggishly to light. There was a right central facial paresis. There was some weakness of the right upper extremity. On the right side there was a combination of absent abdominal reflexes, increased knee and ankle jerks, a poor plantar response and a slight reduction of sensation.

Course. It was felt that there was a lesion in the left cerebral hemisphere in the region of the lower part of the precentral and postcentral gyri. The nature of the lesion was considered to be either a chronic subdural hematoma, a neoplasm or a gumma. The possibility that the symptomatology could be explained on the basis of a luetic vascular lesion was also entertained.

A hyperpnoea test brought on a typical mild attack of aphasia with twitchings of the head, the right side of the face and the right arm. The deep reflexes on the right side were hyperactive during the seizure. This test was taken as confirmatory evidence of the presence of a localized lesion in the region of the left central gyrus.

Exploratory craniotomy over the left parietotemporal region was advised and performed. A large flap was made but despite this the dura mater and the underlying brain were found to be normal and the flap was replaced. Immediately following the operation the patient became aphasic and developed a right hemiparesis. The aphasia cleared up in four days but the right-sided weakness remained. The patient was discharged on April 14, 1933, one month after admission.

Readmission. For six months he appeared to be well. At the end of that time his speech was noticed to become thick and incoherent. The weakness of the right lower extremity increased and was now associated with loss of sensation. He became incontinent. His vision began to fail. When readmitted on October 3, 1934 marked bulging of the decompression area was noted. The left pupil was larger than the right. There was bilateral papilledema with retinal hemorrhages. There was a right spastic hemiplegia. The blood Wassermann reaction was again negative. Encephalographic studies showed displacement of the ventricular system to the right and a small left lateral ventricle. The impression was that of a neoplasm in the left frontotemporal region. A craniotomy was then performed. A large lesion six cm. in diameter and two cm. thick was found straddling the Rolandic area on the left side. It was of firm consistency and a section was reported pathologically as a gumma. It was not removed. Antiluetic treatment was instituted. The patient's condition declined, terminating in death two and one half months after the second operation.

Gross Anatomy. A large tumor, measuring 4 x 3½ cm. was found near the dorsal border of the left cerebral hemisphere in the frontoparietal region. The overlying dura mater was thick and adherent to the surface of the tumor. The center of the tumor was necrotic. (Fig. 15A.) Another tumor was found in the posterior

portion of the right frontal lobe. The mass was cone-shaped with the base lying near the vertex and the apex extending downward into the brain tissue for a distance of 4½ cm. (Fig. 15B.) Another lesion was found in the right occipital region. This measured about ½ cm. in diameter. The base of the brain was free from exudate. (Miliary tubercles were found in the lungs, liver, spleen and kidneys.)

Microscopic Anatomy. The tumor masses consisted mainly of caseous, necrotic material in which very little cellular structure could be recognized. A few giant cells were found. Lymphocytes were present at the periphery and around the
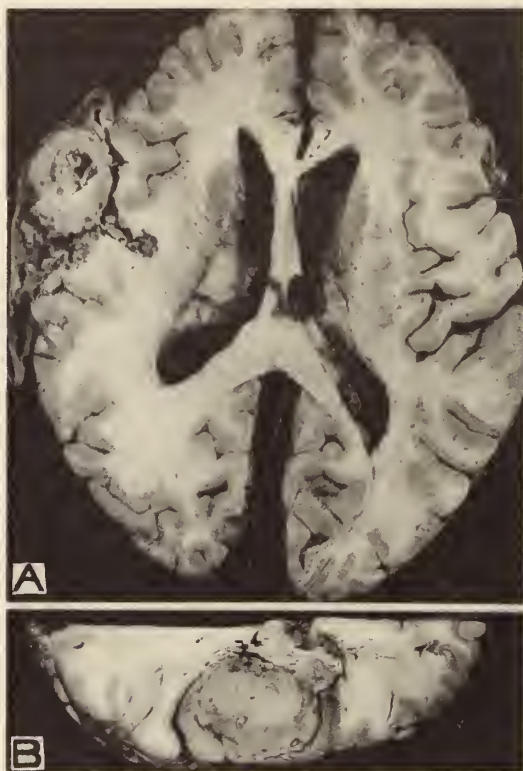
Fig. 15 (Case 11). A. Tuberculoma in left cerebral hemisphere. B. Tuberculoma in right cerebral hemisphere.

blood vessels. Ziehl-Nielson stains revealed a few long, beaded, rod-shaped organisms.

Comment by Dr. Globus. Dr. Beres has stressed the point that there was no meningitis although the tuberculomata were close to the meninges. It is believed by some that tuberculous meningitis is usually the result of a rupture of the contents of a tuberculoma into the subarachnoid space. In a study which is now being completed by Dr. Beres and Dr. Meltzer evidence has been gathered which does not confirm this opinion. This case demonstrates that large tubercles situated close to the surface of the brain, even projecting into the meningeal space, may exist without the causation of tuberculous meningitis and cause death as expanding lesions.

Hermann Goldenberg

October 13, 1862–April 1, 1937

A Tribute by Bernard Sachs

The Thread of our life would be dark,
    Heaven knows!
If it were not with friendship and
    love intertwined.

             —T. Moore

It is a privilege in the presence of the intimate friends of Hermann Goldenberg, and at this solemn moment, to be given the opportunity to pay a final tribute of esteem and affection to him, who has so suddenly been taken from our midst.

In reviewing his career as I got to know him during the last forty years or more, I am doing a service not only to the Dead, but to myself and many others, especially to his medical colleagues, to whom a just appreciation of his principles and his activities will prove to be an inspiring example and a lasting memory.

In the Eighties of the last century, our friend came to this Country at a time when he, like many others, still had reason to be proud of his native land and of his German university training; and yet, from the moment he reached this Country, he was, and ever remained, a staunch American. It was his ambition to be a useful citizen and a credit to American medicine. In both these quests he succeeded admirably.

His absolute honesty of purpose, his reverence for truth, his abhorrence of sham, coupled with an unusual love of his fellow men, made him a splendid member of the community. And, if you will add to these qualities a passion for reading, a critical mind, and a thorough appreciation of scientific achievement, you will readily understand why he became one of the foremost practitioners in his special line of work, and one whom many of us loved to consult.

At Mount Sinai Hospital, at the Academy of Medicine, in private practice, everywhere his advice and his opinion were sought and were appreciated. If he could do any one of his friends, or any patient a real service, it was rendered in that cheerful way of his which especially endeared him to all. "A finished gentleman from top to toe."

He had but one shortcoming. He was modest to a fault. He shrank from publicity, even from participation in medical meetings, where all would have been glad to listen to him, as they always were on those rare occasions when he had the courage to appear. He preferred the life

of the active physician during the day and of the quiet student during the evening.

Everyone has the right to seek happiness and contentment in his own way. For Hermann Goldenberg his home was his castle, and how unselfishly he was guarded by his loving wife and devoted daughter, only those can appreciate, who knew and saw him often in his small family circle. It was this unquestionable devotion that helped our dear friend to bear up bravely during a most trying illness and enabled him to keep up his morale, and to continue his activities to the very end. His sudden death was a mercy to him. He was spared much suffering and his immediate dear ones have the satisfaction of knowing that they enabled him to round out a life of great usefulness and undiminished contentment.

And now, my dear Friend, we bid you farewell. Sincerely and deeply we mourn over you. We are proud and grateful that you have been one of us.

Peace be with you.

This tribute to the memory of a departed friend, delivered by Doctor Bernard Sachs at the funeral on April 4, 1937, expressed so beautifully the sense of loss felt by the colleagues of Doctor Hermann Goldenberg that it was found most desirable to allow it to remain unaltered in the form in which it was spoken.—EDITOR.

ABSTRACTS

Members of the hospital staff and the out-patient department of The
Mount Sinai Hospital are invited to submit for publication in this column
brief abstracts of their articles appearing in other journals.

*Thrombo-angiitis Obliterans (Buerger) XI. Treatment of 524 Cases by Repeated In-
travenous Injections of Hypertonic Salt Solution; Experience of Ten Years.* S.
SILBERT. Surg. Gynec. & Obst. 61: 214, August 1935.

This paper reports the experience of the writer in the treatment of a large series
of patients with thrombo-angiitis obliterans by the method which he introduced in
1923. The technique of injections is described. A portion of the paper is devoted
to the criteria used for differentiation between cases of thrombo-angiitis obliterans
and arteriosclerosis. The rôle of tobacco as the exciting cause of thrombo-angiitis
obliterans is again stressed, and the evidence in support of this relationship is pre-
sented in detail. Follow-up results are given and the importance of a careful fol-
low-up is emphasized. The best single criterion of success in treatment is stated to
be the percentage of amputations required. In patients treated with repeated in-
travenous injections of hypertonic salt solution, only 7.6 per cent amputations were
necessary as compared to 22 per cent in other large clinics. The additional methods
of treatment employed in the healing of ulcers are presented, and the use of periph-
eral nerve section for the relief of pain is discussed. The history of several illustra-
tive cases is given. The writer's conclusions are that thrombo-angiitis obliterans
is not a progressive disease if patients discontinue the use of tobacco, and that re-
peated intravenous injections of hypertonic salt solution is a simple and effective
method of treatment for this condition.

Diagnostic Value of Defects in the Visual Fields and Other Ocular Disturbances. J. H.
GLOBUS AND S. M. SILVERSTONE. Arch. Ophth., 14: 325, September 1935.

This communication was based on an anatomical and clinical survey of 171 verified
supratentorial tumors in an attempt to ascertain what assistance studies of visual
fields and other ocular disturbances render in the localization of brain tumors, how
frequently observations at operation or on post mortem examination corroborate
the clinical diagnosis and what factors aside from location of the tumor are respon-
sible for characteristic ocular disturbances. For this purpose the authors made a
detailed classification of supratentorial tumors according to their exact location in
the brain and further subdivided tumors into two main groups, encapsulated and
infiltrating.

Irregular visual field defects, including bitemporal hemianopia, homonymous
hemianopia and unilateral temporal defects were found with tumors situated close
to the optic chiasm: subfrontal encapsulated tumors, suprasellar meningiomas,
Rathke's pouch tumors, and pituitary adenomas. On the other hand, third ventri-
cle infiltrating tumors did not produce field defects in spite of the close proximity of
these tumors to the optic chiasm. Typical homonymous quadrantic or hemianopic

defects were obtained in tumors involving the temporal lobe with the exception of temporal posterior encapsulated tumors in which the visual field defects were inconstant and not characteristic. Homonymous defects were also obtained in tumors involving the occipital lobe. Of the 171 cases, 99 were situated in the optic pathways but only 41 of these revealed field disturbances which were of assistance in the diagnosis. Failure to obtain characteristic field defects in many cases were due either to marked reduction in vision because of optic atrophy or papilledema, or to poor coöperation on the part of the patient because of intellectual depreciation, mental deterioration or extreme youth. A frequent finding was that in homonymous hemianopic or quadrantic defects, the defect on the side opposite the lesion was almost always greater than that on the same side.

In groups of tumors in which no visual field defects of diagnostic value were expected, the changes were chiefly in the nature of slight contraction of the entire field. There were three cases, however, parietal encapsulated tumors, in which homonymous defects were found.

In the intraventricular and basal ganglion tumors, no predictions could be made but visual field studies in these groups were unsatisfactory.

In observations on papilledema, there were no constant findings. Advanced papilledema was found with frontal lobe tumors as well as with tumors situated posteriorly.

Primary optic atrophy was found in tumors situated near the optic chiasm. Secondary optic atrophy was infrequent. The Kennedy syndrome was observed in only 1 of 40 cases of tumors in the frontal or prefrontal regions.

Diminution of vision was generally found as an accompaniment of optic atrophy.

Of the pupillary manifestations, inequality was of frequent occurrence. The larger pupil was often contralateral to the site of the lesion and homolateral with the visual field defect. Impairment of the light reflex, either unilateral or bilateral occurred most frequently with tumors situated in the sellar and suprasellar regions, and in temporal infiltrating tumors.

Of the other cranial nerves, the abducens nerve was involved in 36 cases, either bilaterally or unilaterally, with no definite relation to localization of the tumor. Oculomotor nerve palsy occurred most frequently with prefrontal and interpeduncular tumors and the involvement was homolateral with the tumor. The trochlear nerve was involved in only one case in which there was complete ophthalmoplegia.

Impairment of convergence was of frequent occurrence and had no localizing value. Conjugate ocular movements were often observed either as spasmodic or paralytic, but in only two cases was the lesion in the frontal lobe; in the others, the lesion was far removed from the second frontal convolution, the center for conjugate movement of the eyes. Impairment of upward gaze was found in 13 cases, all of which were posterior to the frontal lobe. No true nystagmus was seen in any case but nystagmoid twitchings were found in all the groups. A history of transient diplopia was found in 6 cases.

Exophthalmos was noted in the frontal groups, temporal lobar, and third ventricle tumors. Unilateral exophthalmos, when found, was homolateral with the lesion. Inequality of the palpebral fissures, when found, was usually part of a hemiplegic picture, in association with a facial paresis. In cases in which the oculomotor nerve was involved, some gross alterations were noted in the structures neighboring on the aqueduct: gross displacement, distortion, or disorganization of such structures due to the proximity of the neoplasm.

The preoperative period averaged 17 weeks for all the cases. The average for the encapsulated tumors was 73 weeks, and for the infiltrating tumors 13 weeks.

The authors conclude that while the number of tumors in which perimetry was of assistance in the diagnosis was not large, visual field defects, when obtained, form

highly useful leads for the localization of temporal, temporo-occipital and interpeduncular tumors, and they are substantiated by subsequent operative or post mortem findings. Deviations from the characteristic findings may be explained by the infiltrating character of a tumor in which the optic pathways are invaded in an irregular manner. Indirect pressure, particularly when caused by an encapsulated tumor, is another factor.

Gumma of the Heart: Report of Two Cases. A. R. SOHUAL. Arch. Path. 20: 429, September, 1935.

Acquired tertiary syphilitic heart disease (exclusive of aortitis with commissural involvement) is uncommon and consists of circumscribed gummatous myocarditis (cardiac gumma) and diffuse gummatous myocarditis.

The authentic cases of cardiac gumma recorded in the literature have been enumerated; to these, two new cases are added.

Gummatous cardiac aneurysm generally occurs at the base of the left ventricle, where it is particularly apt to interfere with valvular function.

Involvement of the pericardium (especially of the visceral layer) occurs generally by extension from myocardial gummas and less often from gummatous lesions in the roots of the great arterial trunks.

Clinical recognition of the disease is rare. Unusually situated weird stenotic murmurs, unexplained roentgen shadows at the cardiac margins and heart block in a patient in whom syphilis is suspected suggest the possibility of tertiary cardiac syphilis, most likely gumma.

Lesions of the Left Auricle in Rheumatic Fever. L. GROSS. Am. J. Path. 11: 711, September 1935.

Gross and histological observations on the left auricle, based on an examination of 87 rheumatic hearts, are described. The material is classified into five clinical groups, depending on the course of the disease. It is shown that macroscopic lesions of the left auricle occur in 80 per cent of the cases and microscopic lesions in 100 per cent.

In the clinical groups which represented the more active cases the lesions were very varied, generally quite conspicuous and presented a sufficient number of individual pathological processes on which it is possible to make a diagnosis of rheumatic fever. These lesions consist of edema and marked infiltrations of the endocardium with inflammatory cells, the banded appearance of some of these cellular aggregations, the presence of eosinophilic swelling of the collagen, the presence of Aschoff bodies in the endocardium, subendocardium and myocardium, the distortion of the elastic tissue and the widening, hypercapillarization and marked infiltration of the subendocardium. To these, furthermore, may be added the two important features of capillary penetration into the endocardium and the presence of reduplications.

In the more chronic clinical groups, the inflammatory phenomena of the endocardium and subendocardium were present in almost every instance, but very much milder. Aschoff bodies occurred in extremely low incidence or not at all, and the subendocardial inflammatory phenomena were also less frequent and milder, as were those in the myocardium and pericardium. On the other hand, the almost invariable presence of reduplications, sometimes multiple, the penetration of capillaries into the endocardium, when present, the marked hypertrophy of the myocardium and the presence in the majority of cases of some form of pericardial lesion, together with the increase and irregularity of the endocardial smooth muscle, readily constituted criteria on which to entertain at least a suspicion of rheumatic fever.

A description is also given of the age period changes of the normal left auricle, as observed in 50 hearts.

Neoplasms of the Oral and Upper Respiratory Tracts Treated by Protracted Roentgen Therapy. W. Harris. Am. J. Roentgenol. 34: 482, October 1935.

Twenty-six cases of extensive intra-oral and laryngeal carcinoma were treated by protracted roentgen irradiation according to the principles of Coutard. The relative merits of rapid and slow methods of treatment (high and low rates of "r" flux per minute) are discussed. The importance of active supportive treatment during the irradiation is brought out. The best results were obtained in extrinsic larynx lesions. Cure by external irradiation alone is usually impossible in extensive infiltrating lesions of the oral cavity. Supplementary treatment by intrinsic radium or by electrothermic methods must be used to eradicate these lesions. The paper brings out the fact that better results are obtained by the use of the new technique in lesions of the upper respiratory tract.

Ophthalmoscopic Appearance of the Nerve Head in the New-Born and in the Young Infant. S. Karelitz and P. Vogel. Am. J. Dis. Child. 50: 872, October 1935.

The optic disc of the new-born infant may appear gray on ophthalmoscopic examination. This gray color of the optic disc and the pallor of the fundus in the period just after birth and for the first six months of life, and occasionally longer, are associated with physiologic developmental changes which continue for a variable period after birth, usually not longer than six months, except for general pallor of the background of the eye which may be evident for a much longer period.

Retinal pigmentation and vascularization of the nerve and choroid are perhaps the most important factors in the explanation of the grayish color of the optic disc of the infant.

In view of these findings a diagnosis of optic atrophy in new-born and young infants based on grayness of the disc is associated with great possibility of error.

Studies on the Relation of Non-Specific Ulcerative Colitis to Bacillary Dysentery (with Particular Reference to the Dysentery Bacteriophage). A. Winkelstein and C. Herschberger. Am. J. Digest. Dis & Nutrition 2: 408, September 1935.

The authors found bacillary dysentery organisms in 7 out of 60 typical cases of non-specific ulcerative colitis. They also found in the stools a dysentery bacteriophage in 15 of 41 cases of ulcerative colitis.

Furthermore a high agglutinin titer for dysentery organisms was found in 27 of 120 cases. These studies suggest that bacillary dysentery may play an etiologic rôle in some cases of non-specific ulcerative colitis.

The authors discuss further investigative and therapeutic complications of their work.

Angina Pectoris and Heart Block, as Symptoms of Calcareous Aortic Stenosis. E. P. Boas. Am. J. Med. Sc. 190: 376, September 1935.

Angina pectoris and heart block are common accompaniments of calcareous aortic stenosis. On the basis of the prevalent theory that the anginal syndrome is caused by anoxemia or ischemia of the heart muscle, the mechanism in these cases is readily understandable. The blocking of the blood flow to the myocardium takes place at the aortic orifice instead of in the coronary arteries themselves. It impairs the blood supply in the territories of both right and left coronary arteries simultaneously, in contrast to the more localized area of impeded blood flow usually occurring in coronary arteriosclerosis. When the aortic orifice is greatly narrowed, rapidly developing heart failure by still further retarding the blood flow through the minute opening may induce acute myocardial ischemia analogous to that following coronary artery thrombosis and giving rise to identical symptoms. It may be followed by sudden death. Conduction defects in patients with aortic stenosis are not uncommon and are due to extension of the calcareous process to the A-V bundle.

JOURNAL

OF

THE MOUNT SINAI HOSPITAL

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CONTENTS

RUPTURED METASTATIC LUNG ABSCESS FOLLOWING SEPTIC ABORTION

WITH UNUSUAL BACTERIOLOGICAL FINDINGS

JOHN H. GARLOCK, M.D.

[*From the Surgical Service of Dr. Harold Neuhof*]

The train of events in the clinical history of the following case offers a clear-cut picture of the origin, course and subsequent cure of a putrid lung abscess. It is an unique example of an abscess metastatic from a distant focus with bacteriological confirmation.

CASE REPORT

History (R. P., Adm. 386552). The patient, aged 22, was admitted to the hospital on November 9, 1935 and discharged on December 4, 1935. Five weeks before admission the patient had had an induced abortion without anesthesia. Four days later she developed fever, shaking chills, and pain in the left chest posteriorly. Since then this pain had extended anteriorly. In the beginning there was only scant non-foul sputum. Several days later her physician found signs of consolidation in the left lung and made a diagnosis of pneumonia. The septic fever and severe chills continued. Ten days before admission the chest was aspirated and air was removed. The physician did not know whether or not this air was foul. Temperature continued between 103°F. and 105°F. Seven days before admission four c.c. of foul pus were aspirated from the left chest posteriorly. Again, four days later one and one half quarts of foul pus were aspirated. Twenty-four hours before admission the patient began to expectorate large amounts of foul-smelling sputum. Three blood cultures taken at home were reported negative. The latter part of the patient's illness was characterized by extreme dyspnea.

Examination. The patient was desperately ill, almost in extremis. She was markedly dyspneic and cyanotic. There was frequent cough and expectoration of foul-smelling sputum. The teeth and throat were in good condition. The heart was found shifted to the right with the apex 1.5 cm. to the left of the mid-sternal line. The physical signs in the left chest indicated the presence of a large amount of fluid and air. The flat

level by percussion shifted with change of position of the patient.   There
was no clubbing of the fingers.   The patient was too ill for X-ray examina-
tion.   Hemoglobin was 50 per cent.   White blood cells were 15,000:
polymorphonuclear leucocytes 80 per cent.   X-ray examination of the
chest, made two days before admission to the hospital, disclosed an ac-
cumulation of fluid and air in the left pleural cavity, displacement of the
heart to the right, and circular shadows in the right lung which were in-
terpreted as multiple abscess cavities.   (Figure 1.)

Course.   Immediate operation was undertaken.   Under local anes-
thesia, with the patient in a half reclining position, a large section of the
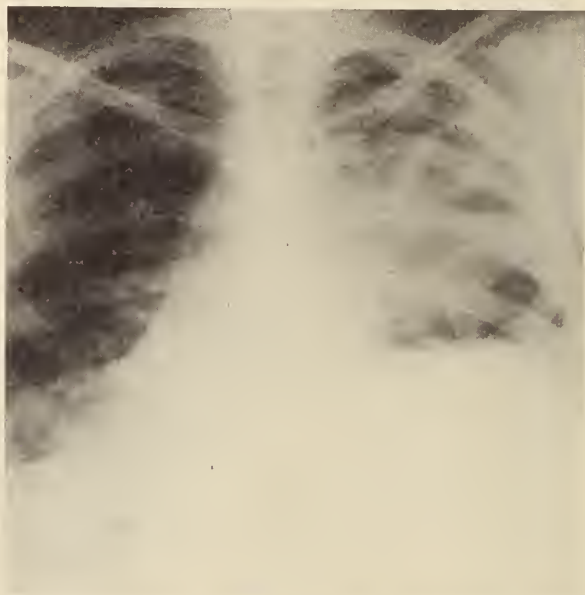
Fig. 1. X-ray plate of the chest taken two days before admission to the hospital.
This showed (1) a large amount of fluid and air in the left pleural cavity, (2) displace-
ment of the heart to the right, and (3) multiple shadows in the right lung which were
interpreted as multiple abscess cavities.

seventh rib was excised posteriorly.   The chest was opened, liberating a
considerable amount of foul-smelling pus and air.   There was found an
almost complete empyema of the left thoracic cavity.   The mediastinal
structures were fixed with exudate.   With the aid of the Cameron light
the operator was able to visualize a punched-out lesion about three quar-
ters of an inch in diameter situated in the upper lobe anteriorly opposite
about the fourth rib.   There was a blowing bronchial fistula in its center.
This cavity in the lung was packed with iodoform gauze, as was also the
empyema cavity.   The patient was given a transfusion of 500 c.c. of
blood.

The patient was placed in an oxygen tent, which immediately relieved the dyspnea and cyanosis. Her recovery was remarkably rapid. The chest packings were removed on the third day, and tubes were inserted for better aeration of the empyema cavity. On the third postoperative day a chest X-ray examination showed some fluid and air in the left chest with a small cavity visible in the parenchyma of the upper lobe. In addition, there were two areas demonstrable in the right lung which were in-
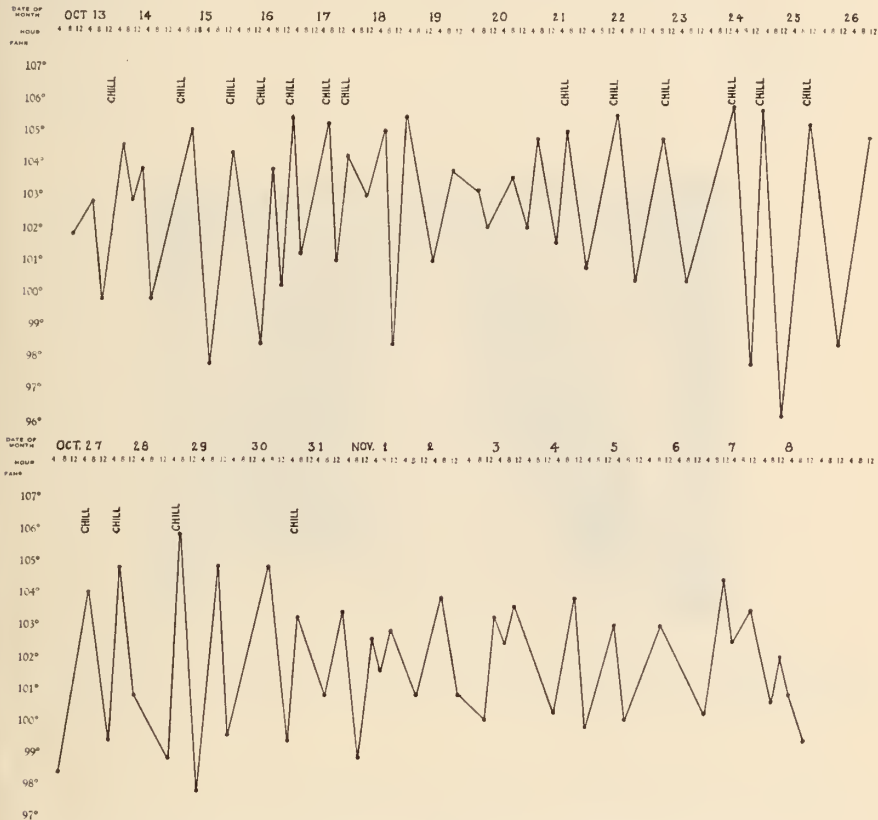

FIG. 2. Temperature chart of the patient before admission to the hospital, indicating the profoundly septic course over a period of twenty-seven days.

terpreted as abscesses. Thick greenish discharge from the vagina, which was noted on admission, continued for about ten days. A note on the fifth postoperative day indicates marked improvement in the general condition of the patient, and gradual disappearance of the physical signs in the right chest. The oxygen tent was discontinued on the fifth day. On the eighth postoperative day the temperature was normal, and there was no cough or sputum. Cyanosis had disappeared, as had also the abnormal physical signs in the right chest.

Culture of the pus removed at the time of operation showed a Schott-meuller anaerobic hemolytic putrid streptococcus and a streptococcus viridans. Culture from the vaginal vault and cervix revealed the identical organisms with the same cultural characteristics. An X-ray examination of the chest, taken twelve days after operation, showed complete disappearance of the shadows in the right lung. (Figure 3.)

The patient was finally discharged a month after admission to the hospital in excellent condition, with marked diminution in the size of the thoracic cavity. She was subsequently followed in the Out-Patient Department.

Follow-up. The patient was last seen approximately seven months after discharge. The chest wound was completely healed. There was

Fig. 3. X-ray examination made twelve days after operation indicating (1) complete drainage of the left pleural cavity, and (2) disappearance of the shadows in the right lung.

no cough or expectoration. She had gained considerable weight and examination of the chest was completely negative.

COMMENT

It is fair to assume from the facts submitted that the source of the pulmonary infection was the original septic abortion. A septic thrombophlebitis either in the uterine wall or the veins of the broad ligament can be postulated. Septic emboli lodged in both lungs, as evidenced by the X-ray findings both before and after the patient's admission to the hospital. One of the emboli found a peripheral localization where it set up a more severe inflammatory reaction and finally, after a peripheral abscess was formed, perforation into the free pleural cavity took place. The re-

sultant pyopneumothorax brought the patient to the hospital and made urgent surgical intervention imperative.

The bacteriological findings in this case are of unusual interest. The culture from the chest pus at the time of operation produced a Schott-meuller anaerobic hemolytic putrid streptococcus and a streptococcus viridans. A smear taken from the vaginal vault and the cervix revealed the identical organisms with the same cultural characteristics. This bacteriological confirmation of the source of the lung abscess, followed by recovery of the patient, is, I believe, an unique experience for the members of the Chest Group at the hospital. It is interesting to note that the blood culture, taken at the time of admission, was negative.

SUMMARY

The unusual features of this case are:

1. Recovery from a severe septic abortion.

2. Metastatic lung abscesses from the pelvic infection.

3. Rupture of a peripherally situated abscess with resultant pyopneumothorax.

4. Cultivation of identical organisms from the pulmonary lesion and the cervical discharge.

5. Resolution and absorption of other more centrally located lung abscesses, as indicated by repeated X-ray examinations.

6. Subsequent complete recovery of the patient.

GONOCOCCAL ENDOCARDITIS WITH JAUNDICE

S. S. LICHTMAN, M.D.

[From the Medical Service of Dr. George Baehr]

In a study (1) of jaundice occurring in patients with heart disease, it was found that this complication was noted but once in fifty-three instances of acute and subacute bacterial endocarditis. The rarity of jaundice in subacute bacterial endocarditis has already been noted by Libman (2) in a review of his vast experience with this disease. A survey of four thousand necropsies performed in this hospital in the past nine years disclosed only one case of jaundice among seventy-five patients who have died from subacute bacterial endocarditis.

CASE REPORT

History (Adm. 390285). A housewife, 56 years old, entered the wards of the hospital complaining of generalized weakness for about five weeks. Four weeks before admission she suffered a rigor with fever as high as 106°F. followed by numerous chills. The day before admission and following a rigor there appeared a shower of small hemorrhagic lesions on the skin over the dorsum of the hands and forearms.

Her familial and previous medical history revealed no significant clinical data. There was no history of recent trauma, infection, cough, urinary symptoms, or bleeding from mucous membranes. The menopause occurred at the age of 46 years.

Examination. The patient, an Italian woman, was extremely pale, and anxious in appearance. She was comfortable in the supine position, and perspired freely.

Signs in the chest indicated the presence of an area of consolidation at the base of the right lower lobe of the lung. Moist râles were present at both lung bases. The heart was not enlarged to percussion. A loud whistling systolic murmur at the apex and a low rough systolic murmur over the pulmonic area were heard. The tip of the spleen was just palpable. The lower pole of the right kidney was ballotable. The pelvic examination was entirely negative. There was no evidence of vaginitis. The finger tips were slightly clubbed. There was slight pre-tibial edema. The skin exhibited showers of petechiae about the knees, elbows, and the dorsal and volar surfaces of both forearms, some with white centers. The systolic blood pressure was 78 mm., the diastolic, 44 mm. of mercury. Fever was of the intermittent type accompanied by frequent sensations of chilliness.

Laboratory Findings. The blood showed a marked secondary anemia, leucocytosis and thrombocytopenia. The hemoglobin was 41 percent (Sahli method), erythrocytes numbered, 3,120,000, thrombocytes, 40,000 per cu. mm.; leucocytes 19,600 per cu. mm. The differential leucocyte count showed 95 percent polymorphonuclear neutrophiles, 2 percent lymphocytes, and 3 percent monocytes. The urine contained albumin and erythrocytes but was free of bile.

The blood Wassermann reaction was negative. The blood chemistry on admission was: urea nitrogen 28 mgm. per 100 c.c., glucose 100 mgm. per 100 c.c., cholesterol 150 mgm. per 100 c.c., icterus index (acetone method) was 9, the Van den Bergh reaction: the direct was negative, the indirect 0.2 mgm. per cent. Two blood cultures proved sterile, a third yielded a slow growing gonococcus.

The electrocardiograph indicated sinus tachycardia, rate 135 per minute, slurring of the QRS complex, and T-waves of low voltage.

X-ray examination of the chest showed accentuation of the markings throughout both lungs with a few mottled shadows in the right lower lobe. The pulmonary vessels at the root of the lung appeared to be dilated considerably. The appearance was that of marked congestion of the lungs with the possibility of an inflammatory process in the right lower lobe.

Course. The condition of the patient grew worse. The temperature fluctuated between 97° and 105°F. There were no distinct rigors. The quality of the apical cardiac murmur changed constantly between a harsh to a whistling or musical systolic murmur. Several days after admission frank purpuric skin lesions appeared over the trunk and extremities. The hemoglobin dropped to 23 percent. On the sixth day skin icterus became definite and bile appeared in the urine. Urobilinogen was present in the urine, one part diluted ten times. The icterus index was 10. The Van den Bergh became delayed direct, bilirubinemia 0.9 mgm. percent. Transfusions restored the hemoglobin to 41 percent but the thrombocytopenia remained as low as 40,000. Shock tenderness developed over the hepatic area. Since the blood cultures had as yet not exhibited the growth of the gonococcus, this sign with jaundice, and intermittent fever suggested the existence of a pylethrombophlebitis with liver abscesses. Exploratory puncture of the liver did not confirm this suspicion, however. A fragment of liver tissue removed by puncture showed the presence of polymorphonuclear neutrophiles and degenerated liver cells. The patient declined progressively and died in pulmonary edema, two weeks after admission to the hospital, and seven weeks after the onset of her illness.

Necropsy Findings. *The lungs* showed pulmonary edema, and no areas of pneumonia. *The heart* weighed 350 grams. The ventricles were dilated. The endocardium of the tricuspid valve was smooth, glistening and translucent with many opaque areas. The valve leaflets were moder-

ately thickened. The chordae tendinae were smooth and glistening; many were thickened and shortened. The endocardium of the right ventricle was smooth, glistening, and moderately thickened. Along the insertion of the posterior and anterior leaflets there were many short, (1–3 mm.) band-like, firm, glistening strands extending from the leaflets to the endocardium. The trabeculae carneae and the papillary muscles were thickened. The ventricular cavity was diminished in size due to marked bulging of the interventricular septum. The pulmonary valve leaflets were thin, translucent and showed no change. The pulmonary arteries showed no change.

The left ventricle was not dilated, its endocardium normal. The free edges of both leaflets of the mitral valve were moderately thickened. At the medial border of anterior leaflet there were many yellowish pink nodular vegetations which extended from the margin of closure to the free edge, measuring approximately 0.5 to 1.0 cm. The surfaces were rough, granular, moderately friable and projected 2 to 3 mm. above the surface. On the posterior leaflet at the lateral border there were three similar nodular elevations of varying sizes (1.5–1.0, 1.0–0.5, 1.0–0.2 cm.) extending from 0.5–1.5 cm. above the surface. These vegetations were yellowish pink, moderately friable, their surfaces rough and granular. Small pin-head sized nodulations extended along the adjacent chordae tendinae in bean stalk form. A smear made from crushings of these showed gram negative diplococci. Bacteriological cultures made from the valve yielded a gonococcus. The endocardium on the ventricular aspect of the mitral valve was normal. The myocardium of the left ventricle was pale brown and presented many yellow streaks. The papillary muscles were markedly thickened. The coronary arteries showed no change.

The Liver weighed 1875 grams, and was soft, flabby, brownish red. The capsule was smooth, glistening and transparent. The edges were moderately rounded and presented many gray glistening linear striations. The surface was flecked by many discrete yellow and grayish yellow pinhead and larger sized subcapsular areas. There were also present many irregular small 1 to 2 mm. sized red areas. On the anterior and lateral surfaces of the right lobe there were three stellate, irregular defects in the continuity of the surface. The sectioned area was moist, edematous, brownish pink red, flecked by many discrete red yellow and yellow grayish areas. The liver lobules were hazy. The portal areas were seen as depressed areas, pin-point in size. The portal vein and hepatic vessels showed no change. The gall-bladder contained thick syrupy bile. The mucosa was finely ridged. The bile ducts showed no gross changes.

Microscopic examination of liver tissue (Fig. A) revealed a loss of the normal architecture. There was necrosis of the individual cells and also of entire lobules. There was marked fatty change in the cells. At the

periphery of the necrotic areas there were numerous polymorphonuclear neutrophiles, leucocytes, lymphocytes, and erythrocytes. The sinuses were dilated and contained pink granular debris. Disse's spaces were likewise widened. Kuppfer cells were prominent and there was marked erythrophagocytosis in these cells.

The Spleen weighed 620 grams. It was very large and adherent to the diaphragm and stomach. The capsule was thickened at these points of attachment. The surface was rough and presented many depressed circumscribed yellowish brown areas. The edges were rounded and presented many lobulations. The sectioned surface was moist, dark red, and presented many map-like yellowish areas. The surfaces of these areas were moderately granular, the edges were red and elevated, the centers
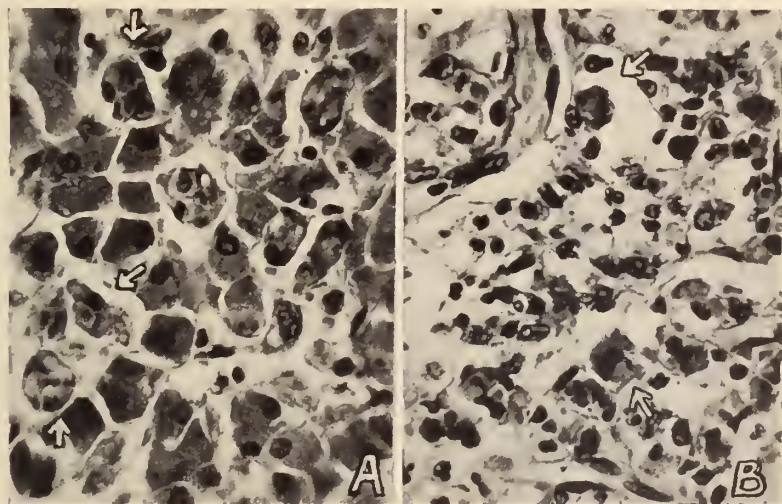
Fig. A–B. Erythromacrophagocytosis in the Liver and Spleen. Microphotographs of the Liver (A) and Spleen (B)

soft, necrotic and yellowish brown. The trabeculae were visible, the follicles were seen as grayish yellow pin points and larger glistening areas. The splenic vessels exhibited no change.

Microscopic examination of this organ (Fig. B) showed moderate congestion with massive areas of necrosis due to infarction. The Malpighian corpuscles were prominent. The capsule was thickened, fenestrated and covered by organized fibrous tissue. There was a small amount of subcapsular hemorrhage. Scattered throughout the follicles and the chords of Billroth were numerous polymorphonuclear neutrophiles, leucocytes, lymphocytes, and plasma cells. The sinuses were empty and the chords of Billroth showed a reticular hypertrophy and erythrophagocytosis. Occasional large macrophages were scattered throughout.

The *Bone Marrow* displayed erythrophagocytosis.

The Kidneys were normal in size and weight. The capsules were smooth, translucent, and they stripped with ease, revealing a smooth, extremely pale yellow surface riddled with pin-point red areas. There was one irregular stellate, depressed area approximately 2 cm. in width. The sectioned surfaces were moist, extremely pale and edematous. The cortex was well demarcated and not narrowed. The pyramids were seen as pale brown areas. The glomeruli were distinguished as red pin-point areas. The mucosa of the calyces and pelves showed no change.

Microscopic examination showed the presence of multiple foci of leuco-cytosis, indicating passage of bacteria. Embolic glomerular lesions were not demonstrable.

The Genital Tract. The uterus was small and firm. The serosa was smooth and glistening. The uterine cavity was slit-like and showed no gross change. The myometrium was normal. The right ovary presented a small cyst with serous fluid. Microscopic examination also did not disclose a focus of infection or portal of entry.

COMMENT

In the case herein reported death occurred three weeks after the onset of symptoms. The clinical course thus was short, yet the pathlogical findings were of the character usually found in the subacute, non-ulcerative variety of endocarditis. Though careful scrutiny of the genital tract, the usual portal of entry for the gonococcus, failed to reveal a recent or healed site of origin of infection, the blood culture leaves little doubt as to the nature of the infection. Bright red petechiae are associated more often with meningococcus bacteremia. However, this type of skin lesion as well as small areas of hemorrhage and even small hemorrhagic vesicles may also occur with gonococcus bacteremia.

The severe anemia was the result of marked blood destruction as evidenced by extensive erythrocyte macrophagocytosis in the liver, spleen, and bone marrow. There was no reticulocytosis in the peripheral blood to indicate active regeneration of erythrocytes. The marked and constant thrombocytopenia with purpura was further evidence of a generalized hematopoietic disturbance. Extensive histological changes and infarctions of the spleen may also have played a rôle in the production of thrombocytopenia.

The jaundice probably resulted from rapid and extensive blood destruction, overactivity of the reticulo-endothelial system, and liver cell damage due to bacterial toxins. The presence of bilirubin in the urine indicates a regurgitation type of jaundice associated with hepatocellular necrosis.

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PRIMARY SARCOMA OF THE LIVER

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Primary sarcoma of the liver is rare. Because of its infrequency, and the puzzling clinical picture frequently associated with it, it is deemed worthwhile to report a case.

CASE REPORT

History (Adm. 392321). The patient, an 18 year old white male, was admitted to the Surgical Service of Dr. Edwin Beer on April 23, 1935. Four months previously the patient had had an attack of severe generalized abdominal cramps which persisted for two days. A laparotomy was done at another hospital and a large "blood tumor" of the liver was found. Further information concerning the operative findings could not be obtained. Two days later, the patient was again operated upon because of hemorrhage from the wound. Two days following the second operation the patient developed severe pain in the right chest and a non-productive cough which was relieved by thoracotomy and tube drainage. Two weeks after the thoracotomy he left the hospital with a well-healed chest wound. He soon began to experience persistent pain in the right half of the abdomen and edema of the lower extremities, the latter despite constant bed rest. In the course of this illness the patient lost thirty pounds.

Physical Examination. The patient was poorly nourished and dyspneic. The scrotum was markedly distended by fluid and there was marked pitting edema of the posterior wall of the thorax, the sacral region and both lower extremities. Over the anterior wall of the abdomen and lower chest there was a wide plexus of distended veins. Signs of fluid were found in the right chest extending up to the angle of the scapula. The heart was displaced considerably to the left. Moderate ascites was present. A firm mass occupying the upper portion of the right half of the abdomen and extending across the epigastrium was palpated. There was marked percussion tenderness in the flanks, loins and costovertebral angles.

Laboratory Data. The hemoglobin was 48 per cent (Sahli); the urine was negative except for a very faint tract of albumin; the blood protein was 5.7 gm. per 100 cc. with albumin 2.3 gm. per 100 cc.; the icteric index was 6; the leucocyte count was 23,300 with 80 per cent polymorphonuclear neutrophiles of which 66 per cent were segmented. The fluid aspirated from the abdominal cavity showed no organisms on culture or smear, while the fluid aspirated from the right chest revealed on culture Streptococcus

hemolyticus and Bacterium Coli. A roentgenogram revealed a shadow in the right chest, with a convex upper border and displacement of the heart to the left. Infrapulmonary effusion, subphrenic abscess or neoplasm below the diaphragm were suggested as the probable causes of this shadow.

Course. The temperature on admission was 102.0°F. and thereafter ran irregularly between 99.0°F. and 103.0°F. Three days after admission, following several unsuccessful attempts to relieve his dyspnea by means of chest aspirations, a thoracotomy was done in the eighth right inter-costal space in the region of the posterior axillary line. A small amount of necrotic tissue was obtained. Biopsied tissue, removed during thora-cotomy at this hospital, was examined by Dr. Paul Klemperer and was reported, "very vascular necrotic malignant tumor." One week later, some material removed from the gaping chest wound was reported, "completely necrotic tumor tissue." Following thoracotomy the patient declined rapidly, became extremely cachectic and died nine days later. The total duration of the illness was five months.

NECROPSY FINDINGS

Gross Anatomy. The body was that of a poorly developed white male. The *face* and the *upper extremities* were gaunt; the *chest, abdomen* and *lower extremities* showed a considerable amount of pitting edema, and the *scrotum* was markedly distended with fluid. In the eighth intercostal space in the region of the posterior axillary line, there was a recent incision, six inches long, through which passed several gauze drains. The base of the wound was made up of soft, grayish black, necrotic tissue. The *ab-domen* was considerably distended and fluctuant. A large number of distended veins could be seen through the skin of the anterior wall of the abdomen and lower chest. The *abdominal cavity* contained about a liter of opalescent, yellowish fluid which clotted partially on standing. The right lobe of the *liver* extended five fingers' breadth below, the left lobe three fingers' breadth below the costal margin. The liver seemed to have been pushed downward and to the left. The right diaphragmatic dome rose to the second, the left to the fifth intercostal space. The liver was very large; it weighed 4300 gm. A mass, the size of a child's head lay within the liver and almost replaced its entire right lobe. This mass bulged from the upper surface of the liver and was so situated that, although it formed almost the entire superior, anterior and lateral sur-faces of the right lobe of the liver, it appeared on the inferior surface only in a small area posteriorly. Wherever the mass was in contact with the diaphragm it was adherent by short, gray, friable bands. On the right surface of the tumor there was an excavation, forming the base of the above-described wound. The intercostal incision did not communicate with the right pleural cavity, owing to the mechanical obliteration of the the right costophrenic sinus. The *tumor* was quite soft and composed of

long, slender, interlacing bands of grayish white medullary tissue frequently mottled by hemorrhages and yellowish areas of necrosis. Also, scattered throughout the cut surface of the tumor mass, there were numerous locules, varying in size from 1 to 5 cm. in diameter. These contained a coagulable fluid of varied hue from an opalescent yellow to a creamy greenish gray. The tumor grossly had no capsule but was nevertheless sharply demarcated
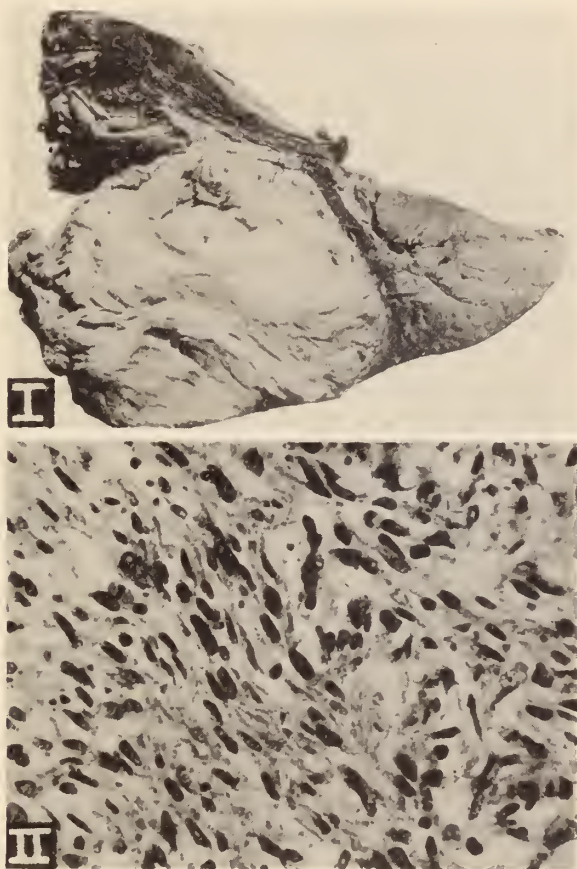

FIG. I. Coronal section of liver showing almost complete replacement of the right lobe by the tumor

FIG. II. Microscopic appearance of a well-preserved portion of the tumor

from the surrounding liver tissue by a hyperemic zone. The left lobe of the liver showed no significant changes. There were recent thrombi in the inferior vena cava below its hepatic portion and in the superior mesenteric vein at its junction with the splenic vein. In addition, the dilated portal vein contained a small parietal thrombus. The retro-esophageal veins, the azygos vein, the hemiazygos vein and the cutaneous veins of the anterior wall of the abdomen and chest were very prominent. There was

marked edema of the lungs with complete atelectasis of the right upper lobe and right middle lobe. The remaining organs were essentially negative.

Microscopic Anatomy. Sections taken from several areas of the tumor and from adjacent liver parenchyma were stained with the hematoxylin and eosin, Van Gieson's, Weigert's elastica, and Mallory's connective tissue stains as well as by the Bielschowsky's silver method and bacterial stain.

The tumor was found to be made up, predominantly, of spindle-shaped cells arranged in an ill-defined whorl pattern, which was best seen in sections taken from the homogeneous medullary portion of the tumor. These cells resembled fibroblasts very closely. They were generally fusiform and contained elongated nuclei poor in chromatin. However some of these spindle cells often had a large long vesicular nucleus with a small amount of chromatin at each end and again, at times, a small round nucleus with considerable chromatin. There were many mitotic figures. In addition to the spindle-shaped cells, there were some round cells and many giant cells with one or more dense nuclei. In some of the giant cells there were hyaline, pink, cytoplasmic inclusions. There was a moderate number of thin-walled capillaries scattered among the tumor cells, the latter having no characteristic arrangement about these vessels. There was considerable hemorrhage with necrosis throughout the tumor; in some of the necrotic areas there were polymorphonuclear leucocytes and gram positive cocci in short chains and clusters. At the periphery of the tumor there was, in some places, a thin fibrous capsule. In other areas, however, the tumor tissue infiltrated moderately the adjacent liver parenchyma without demonstrable vein or bile duct invasion. Everywhere the liver tissue adjacent to the tumor was compressed and atrophic, with areas of hemorrhage and degeneration. The Van Gieson and Mallory stains revealed fine collagenous fibers among the tumor cells.

DISCUSSION

Many observers, impressed by the number of vessels in these tumors and the frequent grouping of the tumor cells around them, have designated as angiosarcoma or endothelioma, neoplasms which are, in fact, fibrosarcomas or fibroblastic sarcomas. On the other hand, there are reports in which the diagnosis is based on the results of intra vitam liver puncture or on incomplete autopsies. It is not improbable, therefore, that some instances of so-called "primary" sarcoma of the liver in the infant are actually metastases from a neuroblastoma of the adrenal; and that most, if not all, of the so-called "primary" melanosarcomas of the liver originate in the eye or the brain. In fact, Herxheimer (12) who reviewed all the cases of reported primary liver sarcoma, published before 1926, accepts as valid only 67 of the 149 recorded cases.

The case reported here closely follows in its anatomical features a majority of the accepted cases of primary sarcoma of the liver. It is a huge nodular tumor of the right lobe of the liver which is macroscopically well circumscribed. There are many large areas showing regressive changes, leading to the formation of cyst-like spaces. Extensive bleeding into the peritoneal cavity following the rupture of such a cyst has been reported by Herxheimer (12). In the present case, as in more than 50 per cent of the reported cases, there are neither metastases nor invasion of the porta hepatis. However, metastases to the adjacent lymph nodes, peritoneum, mesentery and lungs may occur (Herxheimer). Microscopically, the tumor, in the case presented here, is a spindle cell fibroblastic sarcoma with pleomorphism and numerous giant cells. The paucity of collagen and ill-defined whorls of cells, predominantly spindle-shaped, are quite typical of this tumor form. However, cases have been reported quite frequently, in which tumors were rich in collagen, or in which the structure was alveo-lar rather than whorled. In many cases the tumor cells were predomi-nantly round; in some the cells are both of the round and spindle-shaped types.

Despite the fact that the tumor always appears to be well circum-scribed grossly, it is very prone to infiltrate the liver parenchyma and to invade the liver venules and capillaries. Invasion of the former may lead to the formation of tumor nodules such as are frequently found adjacent to the main mass of the neoplasm; invasion of the latter may give rise to an alveolar appearance which has frequently led to the diagnosis of endo-thelioma or angiosarcoma.

Two-thirds of the accepted cases of primary sarcoma of the liver, as well as that reported here, were found in males. The development of ascites was an important feature of the clinical picture. However, icterus and splenomegaly, which were frequently noted in other cases were absent here. Only 5 per cent of the cases occurred between the ages of 10 and 20 years. Most of the cases were found during the first (25 per cent) and seventh decades (20 per cent).

The tumor usually grows very rapidly and the history of disability before fatal termination may be no more than three weeks (Bender (2), Car-michael and Wade (6)). In the case reported here, the first clinical mani-festation was pain in the abdomen, five months before death.

The exact site of origin of sarcoma of the liver is not known, chiefly because the growth is not discovered until quite large and the source there-fore impossible to determine. However, mesodermal tumors of the liver are derived either from Glisson's capsule, the connective tissue of the portal fields, or from the blood vessels, since these are the only structures which develop from the mass of splanchnic mesoderm into which the entodermal liver bud grows (Arey (1), Ewing (9)). Demal (quoted by Ewing) believed that these tumors arise from the normal connective tissue

of the liver.   Others (Delepine (7)), basing their contention on the resemblance of the tumor to endothelioma and angiosarcoma, implicated the cell elements of the vessels as the source of primary sarcoma of the liver. Ewing does not believe that a true angiosarcoma arising from the blood vessels has ever been demonstrated in the liver.

There is no reason to assume that the origin of all the primary sarcomas of the liver is the same, or that the tumor must arise from normal connective tissue elements.   In fact, the maximum incidence of primary sarcoma of the liver is in such different age groups (first and seventh decades) that a different genetic basis for these tumors may be likely.

Herxheimer (12) suggests the following theories of pathogenesis of the tumor.   First, since primary sarcoma of the liver is so frequent in the first decade and even in the first year, some of these neoplasms are congenital, that is, related to some anomalous development of the connective tissue of the liver.   The anomaly differs from that which gives rise to the rare mixed tumors of the liver in infants (Osterman (14)).   Secondly, since a cirrhotic process of the liver is associated with the primary sarcoma in one-third of the cases occurring in adults, he considers cirrhosis of the liver to be a presarcomatous change.   Such an association with cirrhosis might explain the sex incidence of the tumor.   Cirrhosis was not found in the present case.   Further, some authors believe that sarcoma of the liver in humans can arise from the inflammatory connective tissue of a luetic scar and from the capsule of an ecchinococcus cyst or of a chronic liver abscess.   (Hedren (11), DeVecchi (8), Goldstein (10)).

Primary sarcoma occurs not only in man but also in the animal.   It is known to occur in the ox, the dog, the chicken and the rat.   In the rat, the tumor is a spindle cell sarcoma which arises from the wall of a cysticercus fasciolaris cyst (the encysted larva of Taenia crassicolum) in the liver of a heavily infested animal (Bullock and Rhodenberg (5), Brumpt (3), Liang (13)).   Such primary sarcomas of the liver rarely occur spontaneously, but can be induced readily by feeding rats large doses of cat feces contaminated with T. crassicolium eggs and thus infesting their livers heavily (Bullock and Curtis (4), Brumpt (3), Liang (13)).

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ATYPICAL RAYNAUD'S DISEASE

P. GOOLKER, M.D.

[From the Neurological Service of Dr. Israel Strauss]

The term "Raynaud's disease" is used loosely and probably includes a number of quite distinct maladies. The various cases reported have in common what has been termed "Raynaud's phenomenon." The latter may be defined as the intermittent closure of small arteries, such as the digitals, and manifests itself clinically by discoloration of the affected parts. The following criteria have been stressed as essential for the diagnosis of Raynaud's disease: (1) intermittent attacks of discoloration of the extremities; (2) absence of evidence of organic arterial occlusion; (3) symmetrical or bilateral distribution; (4) trophic changes which, when present, are limited to the skin without producing gross gangrene.

The case reported conforms to these diagnostic criteria and represents in addition an unusual feature in the form of definite extensive sensory disturbances.

CASE REPORT

First Admission:

History (Adm. 396564). An unmarried male, 43 years of age, was admitted to the service of Dr. Lewisohn on October 26, 1930. He was a native of Russia and had been in the United States for thirty years. A cousin, also Russian, is said to have had a disorder similar to that of the patient. A brother suffered from pains in the legs but did not develop blisters. The patient had been a moderate consumer of cigarettes until recently and also imbibed alcohol temperately. In his youth, periods of hyperactivity and dissipation alternated with periods of depression in which he entertained suicidal ideas. He shifted his place of residence from city to city and did not marry because of his leg condition and "weak lungs." During cold weather his fingers and toes would become cold, blue and painful. This became more marked in the last two years before admission. On rare occasions, he experienced cramps in the right leg during sleep. In 1910, at the age of 23, and again in 1917, when he was 30 years old, he was confined to tuberculosis sanitaria, but there is no history of positive sputum. X-ray examination of the chest in 1931 revealed some fibrosis in the right apex.

At the age of 24, a blister developed on the plantar surface of the right big toe. Despite various therapeutic measures, it ulcerated and would not heal. After seventeen years, the toe was amputated and recovery was

rapid and uneventful. Six months later, however, a blister appeared on the second toe of the right foot and also ulcerated. The pain that it caused was slight and transient in character. Nine months later, the terminal phalanx of this toe was removed, and although healing occurred, an ulcer developed on the plantar surface of the amputated stump after another nine months.

Examination. A small ulcer was found on the plantar surface of the proximal phalanx of the second toe of the right foot. Both feet were abnormally warm and the toes were hyperemic. All arterial pulsations were normal. X-ray examination of the feet showed some degree of atrophy of the terminal phalanges, particularly on the right.

Course. Conservative treatment with carbon-arc light produced healing of the ulcer in two weeks and the patient was discharged from the hospital.

Second Admission:

The patient was well for a few months but soon began to suffer from pain in the lumbo-sacral region, for which he was fitted with a brace. At times, his legs would fall asleep and become numb and painful, and at times on resting in bed, he sometimes experienced painful cramps in the calves. Four years after his first residence in the hospital, (February, 1935) an ulcer developed on the second toe of the left foot. The patient was readmitted to the Neurological Service of Dr. Israel Strauss.

Reexamination. The patient's blood pressure was found to be 124 mm. of mercury systolic and 84 mm. of mercury diastolic. The peripheral pulses were freely patent. The right big toe and distal phalanx of the second toe were missing and the nails appeared atrophic. There was an oval ulcer, .5 cm. in diameter on the plantar surface of the left big toe. The feet were cold, revealed excessive perspiration, and were duskily cyanotic when dependent and cadaverously white when elevated. The hands were cold, slightly cyanotic and moist with perspiration. Capillariscopic studies revealed changes suggestive of Raynaud's disease: the arterial capillary limbs were very narrow, the blood current was interrupted in many places, the venous limbs were markedly distended and the blood flow varied from loop to loop (sluggish in most and fairly rapid in only a small number).

The deep reflexes were depressed. The sensory disturbances included diminished pain and temperature perception below the knees but almost complete anesthesia over the distal parts of the feet and toes. Touch perception was impaired in the same areas to a lesser extent, vibration sense was diminished below the fourth lumbar vertebra and position sense was impaired in the toes, especially on the left.

Laboratory Data. X-ray examination of the spine revealed a partly sacralized fifth lumbar vertebra and a hypertrophic spondylitis involving

most of the dorsal and some of the lumbar vertebrae.   There was definite lipping of a number of dorsal vertebrae.   The examination of the blood revealed hemoglobin 85 per cent; red blood cells 4,100,000; white blood cells 6,200: 64 per cent polymorphonuclear neutrophiles, 36 per cent lymphocytes.   The blood phosphorus was 3.75 mgm.; blood calcium 10.5 mgm.; blood Wassermann negative.   The urine was essentially negative except for positive lead and arsenic tests.   Gastric analysis revealed no abnormalities.   The spinal fluid revealed an initial pressure of 140 mm. of water and a total protein of 37 mgm.   The serology was negative.

Oscillometer Readings:

	Forearm	Wrist	Calf	Ankle
Right	4	2.5	8	4
Left	3.5	3	8.5	3

Course.   On November 27, 1935, the patient was given .1 gram Mecholyl (a form of acetylcholine) subcutaneously.   About two minutes later, he became flushed, perspired freely and described a feeling of warmth. His pulse was found to be weak and revealed a rate of sixty per minute. The blood pressure readings were 80 mm. of mercury systolic and 50 mm. of mercury diastolic.   The patient vomited repeatedly.   In the course of a few minutes, however, the blood pressure began to rise and the patient recovered.   Because of the reaction, further injections of Mecholyl were not given.   The patient was then subjected to a course of intravenous typhoid injections.   Subsequently, the acral cyanosis diminished and the ulcer healed, but the neurological signs remained unchanged.

Discussion.   A disturbance allied to Raynaud's disease appears to be the most likely diagnosis.   The sensory changes are best explained on the basis of involvement of the peripheral nerves secondary to vasomotor disturbance.   The possibility of syringomyelia is unlikely because of absence of true dissociation of sensation and absence of muscle atrophy, as well as the sparing of the pyramidal tracts in an illness of many years' duration.   In spite of the presence of lead and arsenic in the urine, it is not likely that they are of any etiologic significance as the general clinical course militates against a diagnosis of such forms of intoxication.   Moreover, there is no other evidence of arsenic poisoning, such as exfoliative dermatitis, and biopsy of the skin did not reveal pathological quantities of lead.   The finding of traces of metal in the urine is probably attributable to the patient's consumption of a considerable amount of unwashed raw fruit.   It is, however, noteworthy that Arthur F. Kraetzer (1) has reported five cases of Raynaud's disease which showed arsenic in the urine and which improved under treatment with sodium thiosulphate.   As a result of these findings, he suggested that arsenic poisoning might be an etiological factor in Raynaud's disease.   Pain was not a prominent complaint in the history of this case.   Some authors (Oppenheim, (2), Cassirer, (3), Buerger, (4)) stress intense pain in the affected extremities as an

important symptom of Raynaud's disease, while others (Allen and Brown, (5)) believe that severe pain during the attacks is exceptional and that its presence even militates against a diagnosis of primary vasomotor disturbance of the spastic type.

The objective sensory disturbances from the knees down, such as occurred in this case, are rather unusual for Raynaud's disease. As a rule, objective sensory changes are absent, or, when present, may be limited to the parts affected by the syncope and are not present during the free intervals. The sensory changes are variable when they do occur and may not persist throughout the period of observation. They are most commonly hypesthetic or anesthetic in character and are not radicular or peripheral in type of nerve distribution. Pathological changes in the nature of a neuritis have been found in a number of cases (Cassirer, (3)).

Many varieties of treatment are used for Raynaud's disease. Roentgen therapy has been employed in the hope of influencing the sympathetic nervous system. Glandular extracts have been used and some patients have been advised to live in warm climates and avoid emotional strain. Allen and Brown (5), however, believe that sympathetic ganglionectomy is the most satisfactory method of treatment. They have had gratifying results, especially in the uncomplicated cases, i.e., those showing only recurrent episodes of discoloration of the digits. Lumbar ganglionectomies have been found more successful than cervico-dorsal ganglionectomies. Allen and Brown are convinced that if the sympathetic control is entirely removed in uncomplicated cases of Raynaud's disease in the lower extremities, the result will be a cure. They go as far as to assert that if a return of the malady follows sympathectomy, "one must believe that the operation was incomplete or that the diagnosis of uncomplicated Raynaud's disease was erroneous." A similar view is taken by James C. White (6) and others. Although this patient's condition has advanced from the uncomplicated stage and has probably lost the prospect of a cure, a lumbar ganglionectomy is contemplated to obtain as much relief as possible by excluding faulty vasomotor innervation.

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SICKLE-CELL ANEMIA IN AN ITALIAN CHILD

A Case Report

SAMUEL B. WEINER, M.D.

[From the Pediatric Service of Dr. Bela Schick]

History (J. Z., Adm. 396198). This patient was admitted to the Pediatric Service on July 23, 1936. The child is a white male of eight years, born of Italian parents. His physician referred him to the hospital because of anorexia of three weeks' duration, transient abdominal pain which he had experienced two days previously, and the presence of an enlarged spleen on examination.

The family history has been carefully investigated. The father is 39 years old and the mother is 38 years old. Both appear to be normal, healthy white adults, with no negro features. They were both born and raised in the town of Mistretta, Italy (Sicily). They can trace their family back two generations in this town. They say that negroes were unknown in this town and were only seen with the circus. The parents are certain that there is no negro blood in the family. After coming to this country they had four children, all healthy and well except this patient. There are no familial disease tendencies and no history of icterus, anemia or lues in the family.

The child was born in Passaic, New Jersey, a full term, normal delivery. The birth weight was 3375 gm. (7½ pounds). No cyanosis, convulsions or icterus were present at birth. The child was breast fed for sixteen months. He had no orange juice or cod liver oil during infancy. Vegetables, cereals, eggs and meats were begun during the first year. The child's development has been normal. He sat up at six months, walked and talked at one year. His first tooth appeared at eight months. He has gained in weight steadily and has been progressing satisfactorily in school. Vaccination for smallpox was unsuccessful. The child has been immunized against diphtheria.

The child has had numerous illnesses. At eighteen months of age he had fever on alternate days for one month. At that time he was not seen by a physician. He was weak for some time following his illness. At five years of age he was in bed for three weeks with abdominal pain. No diagnosis was made. Several weeks later he had some epistaxis and because of the anemia present he was given a tonic. At six years of age he was in bed for one week with muscular and joint aches and pains. At that time rheumatic fever was diagnosed. The following year pain in the

knees recurred, and a "swollen" spleen was also found. He was given a series of injections of some medication then. At seven years of age he had mumps, apparently uncomplicated.

One month prior to admission the child had swollen knees for three days with pain and fever. No jaundice had ever been noted.

Examination. Physical examination revealed a well developed and well nourished white male, not appearing ill. No negroid features were present. Standing height was 64 cm., sitting height 132 cm., weight 292. kilo (64 pounds 4 ounces). The skin had a slightly icteric tint. No petechiae or ecchymoses were present. There was no adenopathy. The skeletal system was normal and well developed. The abdomen was slightly distended. The spleen was 4 cm. below the costal margin. The chest examination was negative. No cardiac murmur or enlargement was present. The sclerae were subicteric and the mucous membranes were pale. Genitals were normally developed.

The routine blood examination showed: Hemoglobin 55 per cent; red blood cells 5,190,000; white blood cells 6,700, polymorphonuclear neutrophiles segmented type 47 per cent; non-segmented 10 per cent, myelocytes 1 per cent; lymphocytes 42 per cent. No malarial parasites were seen, even after injection of adrenalin. Because sickle-cell anemia had been suspected a wet preparation was made, and discarded when no sickling was present after two hours. The icteric index was 13. The Van den Bergh test was positive indirect 1–130 (.75 mgm.). Direct Van den Bergh test was negative. Blood cholesterol was 190 mgm. per cent. The blood Wassermann test was negative. The urine showed no albumin, sugar or formed elements. Bile was absent. Urobilin was present 1–20. The Takata-Ara test for liver function was negative. X-ray examination of the chest was normal. X-ray examination of the long bones showed no abnormality of their structure. The electrocardiogram was normal. Sedimentation time was prolonged to six hours (normally one hour). The Schick test and O. T. 1–100 were negative.

Because of the obscure cause for this child's jaundice and anemia, the Hematology Department was consulted. A blood examination by Dr. Vogel on July 28, 1936 showed: Hemoglobin 55 per cent; red blood count 5,450,000; platelets 280,000; white blood cells 7,200; polymorphonuclear neutrophiles segmented type 48 per cent; non-segmented type 8 per cent; lymphocytes 39 per cent; eosinophiles one per cent; monocytes 4 per cent; reticulocytes 5 per cent. The Fragility test showed increased resistance of the red blood cells to hypotonic saline.

No Hemolysis.. .72–.40
Partial Hemolysis... .36–.24
Complete Hemolysis.. None

Sternal aspiration showed a normoblastic marrow. A wet preparation showed beginning sickling after fifteen hours and marked sickling after

twenty-four hours (40 per cent). After thirty-six hours 60 per cent of the red blood cells were sickle-shaped.

On the basis of these findings a diagnosis of sickle-cell anemia was made. The child is being observed in the hospital at present. The spleen has diminished somewhat in size. Saccharated ferrous carbonate 1.00 gm. is being given three times daily. After a week's treatment the hemoglobin is 60 per cent and the red blood cells 4,440,000. Should the child not respond to iron therapy, liver extract and transfusions will be tried. Some success has been reported with splenectomy in these children and we may resort to this. The bloods of the parents, the maternal grandmother and sister have been examined for sickling but none was found after seventy-two hours. Two younger brothers showed sickling, anemia and splenomegaly.

COMMENT

We have presented a case of sickle-cell anemia in a white child of Italian descent. This is the first white child with this disease admitted to our service.

Sickling of the red cells occurs in about 7 per cent of normal healthy negroes with no anemia or other symptoms. Lawrence has also reported sickling in some healthy whites. Most writers believe this is a dominant hereditary characteristic transmitted according to Mendelian laws. When in addition to the sickle cells, a hemolytic anemia is also present, the clinical picture is called sickle-cell anemia.

This disease has been chiefly found in the colored race and was at first believed to be limited to the negro. Males are more frequently affected. The anemia is moderate and only at times is severe. An increased tendency to infections of the respiratory tract is present. These children are weak and have repeated illnesses. Periods of unexplained fever occur. Abdominal pains are frequently seen, with vomiting at times. Joint pains and joint swelling occur in most of these children and for this reason they are often considered as suffering from rheumatic fever. Some children have indolent leg ulcers. Malnutrition is usually present. Very often the icterus is not noted by the parents. The principal physical findings are a subicteric tint to the skin and sclerae. The spleen and liver are usually moderately enlarged. Heart murmurs are frequent, most often due to the anemia. Infantile genitalia were found in a few cases.

The diagnosis is established by examination of the blood. In addition to the low hemoglobin, sickling of a large percentage of the red cells is present in a wet preparation. There is usually increased resistance of the red blood cells to hypotonic saline. The icteric index is elevated and the Van den Bergh test, positive indirect. X-ray examinations of the long bones sometimes show some decalcification and widening of the marrow and a few authors believe this is the cause of the articular pain.

Since 1925 several reports describing sickle-cell anemia in the white race have appeared. The following authors have reported:

1925—Castana—Italian child

1926—Archibald—Arabian child

1927—Stewart—Cuban child (octaroon features)

1929—Cooley and Lee—Greek child

1931—Sights and Simon—American adult of Scotch Irish descent (also had malaria and lues)

1932—Rosenfeld and Pincus—Italian child

1933—Clarke—Two Italian children

1934—Cooke and Mack—Two American children

1935—Wallace and Killingsworth—Two Mexican children and their mother

Pincus and Rosenfeld are inclined to explain the occurrence of this disease in the white race on the basis of admixture of negro blood in the family at some time in the distant past. Cooley and Lee suggest that the disease be looked for in the Mediterranean races where peculiar hemolytic anemias have already been found.

In our case sickle-cell anemia was suspected because of the combination of joint and abdominal pains with anemia and jaundice. Had we examined our wet preparation for sickling for twenty-four hours instead of for two hours, we would have reached the diagnosis sooner. Although all authors have emphasized the fact, it is not generally appreciated that a wet preparation should be observed for twenty-four hours before being sure that the case is not sickle-cell anemia.

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OSSIFICATION OF THE STYLOID PROCESS

LOUIS KLEINFELD, M.D.

CASE REPORT

Dr. M. B., the patient, a surgeon had undergone a tonsillectomy five years ago. The tonsillectomy was performed by me under local anesthesia; the usual dissection and snare technique was used. Throughout the procedure the patient complained of much pain, which could not be relieved by generous additions of novocaine. At the same time, I noticed that when the suction tube was put into the tonsil fossa, there was an audible click. Examination showed that the tonsil fossa was drawn inward and divided into two shallow cavities by a spine, obviously an ossified styloid process. It was then realized that the pain of which the patient complained was referred to the base of the skull, rather than to the region of the pharynx. Obviously, each time the tonsil fossa was touched, pressure was exerted on the styloid process which was transmitted to the point of origin of the styloid process at the base of the skull. A similar condition was encountered on the opposite side. Hemostasis was secured with some difficulty due to interference by the styloid process with the ligatures. The subsequent recovery was uneventful. In fact, much against my wishes, the patient returned to active work in about four days.

At present, five years after the operation, the fossae look fairly smooth, having filled up during the last few years. However, an elevation caused by the styloid process can still be seen and felt in the fossa on one side, and in the anterior pillar on the other.

COMMENT

Normally the styloid process is a thin, bony spine about an inch long, extending downward, forward and inward from the base of the petrous pyramid, just in front of the facial nerve as it emerges from the stylomastoid foramen. The tip of this process, which is sometimes jointed, is cartilaginous and gives origin to the stylohyoid and stylomandibular ligaments, as well as the stylohyoid and styloglossus muscles. (The stylopharyngeus arises from its base.) Embryologically, this process is developed from the second visceral arch.

Ossification of this structure may occur, and extend down as far as the lesser cornu of the hyoid bone. (This occurs normally in dogs.) In some cases the ossified tip extends inward toward the pharyngeal wall to an

abnormal extent. In such a case, the tonsil fossa and pillars will be encroached upon, and may at times provoke clinical manifestations or give rise to some difficulty during tonsillectomy.

Ossification of the styloid process was first mentioned in the literature about three hundred years ago. Resection of the tip was performed as long ago as 1870. About fifty cases of ossification have been reported, in half of which the condition has been bilateral. It occurs about three times as often in men as in women. The right side is affected somewhat more often than the left.

This condition is to be differentiated from the occurrence of small masses of bone and cartilage in the tonsil, either developmental in origin or possibly due to metaplasis of connective tissue.

Clinically, most cases of ossified styloid processes are found accidentally during tonsillectomy. However, they sometimes do give rise to symptoms before operation, such as pain on swallowing, radiating to the ear. In other cases, the patient may experience the sensation of a foreign body in the throat.

Theoretically, the styloid ossification might undergo necrosis during coagulation of the tonsil by diathermy. Tonsillectomy, in the presence of this condition, has led to various complications. Fowler (1) reports a case in which tonsillectomy was followed by paralysis of the glossopharyngeal nerve, due to compression of the nerve against a long ossified styloid process. Fracture of such a process may occur during tonsillectomy, and Babbit (2) reported the occurrence of spontaneous fractures.

The existence of an ossified process may be disclosed by bimanual palpation. A bony spike may be felt which rotates with movements of the head. The diagnosis can be verified by x-ray examination. In most cases, there is no need for therapy. Occasionally there is sufficient annoyance to warrant a tonsillectomy and exposure of the styloid process by a small incision through the capsule. The muscles at the tip can then be dissected off and the projecting part resected. This procedure is not entirely free from danger, and an ascending infection should be guarded against.

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RECTAL INSTILLATIONS OF COD-LIVER OIL IN THE TREATMENT OF ULCERATIVE COLITIS

ROSE SPIEGEL, M.D.

From the Out-Patient Department, Gastro-Intestinal Clinic

Several reports were published in 1935 concerning the local effects of cod-liver oil in the stimulation of the healing of wounds and burns. The effects, encouraging regeneration and epithelialization of tissue at the site of application, were ascribed to the action of vitamins A and D, especially to that of A. The other constituents of the oil were considered to have a minor adjuvant action. The question arose, whether cod-liver oil might not have a similar action on the diseased mucous membranes in patients with ulcerative colitis. Thus this form of therapy was employed in a number of cases. At the time this study was begun, in October 1936, there were no published reports of the use of fish liver oils in the manner to be described in this paper, as far as careful search disclosed. However, on June 7, 1937, at the American Proctologic Society, Dr. Russell Best, in a paper which I discussed, reported on cases treated irregularly with very small instillations of cod-liver oil in conjunction with many other types of therapy.

The Clinical Material. Eleven patients suffering with ulcerative colitis have been observed, for the most part in the Gastro-Intestinal Clinic of The Mount Sinai Hospital, since October 1936. In three of the patients the study was begun on the wards of the hospital. One patient was observed at the Montefiore Hospital through the courtesy of Dr. John Kantor. Dr. Winkelstein and Dr. Yarnis have checked the patients sigmoidoscopically and clinically and I am appreciative of their cooperation in this study.

Form of Medication. A 40 per cent emulsion of cod-liver oil, acacia, and water was used for the most part. The emulsion was considered the preferable form to facilitate the contact of the oil with the intestinal mucous membrane which is bathed by an exudate of pus, mucus and blood, as well as feces. This emulsion is a slow-pouring fluid. It is kept cold and, preferably in flint-colored glass to preserve the relatively unstable vitamin A.

For those patients whose lesions had healed, leaving only a slight residuum in the anal portion of the rectum, large suppositories consisting of 68 per cent cod-liver oil were devised for very localized application.

Mode of Administration. At the beginning of the course of treatment 2 to 4 ounces of the emulsion were instilled slowly into the rectum to accustom the patient to retain fluid as long as possible. Generally, by the end of the first week, the patient could retain 4 to 8 ounces for at least one-half hour and generally for several hours. In about two weeks 8 ounces could be retained overnight. The routine has been to administer 4 to 8 ounces to the recumbent patient, by means of the Murphy drip or a partly clamped enema bag, two to four times a day, depending on individual considerations.

An X-ray examination of one patient twelve hours after the instillation of a mixture of the emulsion and lipiodol to make 8 ounces showed that the material had reached to the middle of the transverse colon. A 4-ounce mixture of the emulsion and barium reached half-way up the descending colon four hours after instillation in another patient.

Control Period of Observation. The patients were observed during a preliminary control period of several weeks to several months in which other forms of medication were used,—injections of carbarsone, emetine, B. coli vaccine, rectal instillations of tannic acid or of quinine bisulphate solution. Several patients had had rectal instillations of various oils, including irradiated oils.

The patients to whom the cod-liver oil treatment was administered were those who had not responded to the control medication as found by sigmoidoscopic examination, the number and character of stools, and the constitutional symptoms. The bland diet of the control period was continued. Tinctura opii was used only infrequently. Three of the patients who had been hospitalized received transfusions.

The duration of the illness has ranged from ten months to nine years. In only one patient was the number of stools at the beginning of therapy less than four. The stools of all the patients were watery or barely formed, and contained gross blood, mucus and pus. The typical sigmoidoscopic findings were hyperemic, puffy, granular mucosa, containing numerous ulcerations covered with hemorrhagic exudate; the mucosa was friable and oozed blood on being touched with the cotton. These findings varied only slightly from patient to patient.

In five of the patients X-ray evidence of ulcerative colitis was present. In the others there was no evidence of organic disease of the colon after barium enema, though extensive lesions of the mucosa were seen on sigmoidoscopy, and clinical signs and symptoms had been present for years.

Response to Therapy. Nine of the eleven patients improved. The first change noted sigmoidoscopically occurred between the first and third week of treatment and was recorded as follows: "The mucosa has less tendency to bleed, definitely paler." The stools began to thicken, and diminish in their content of blood, pus and mucus between the second and fourth weeks. The first indisputable sigmoidoscopic improvement occurred at the end of the first month,—"There are still a few scattered superficial ulcerations

and patches of purulent exudate; rest of mucosa is paler." By this time the number of stools in this group ranged from 1 to 4 per day instead of from 4 to 10. They were formed or semi-formed, contained no blood on guaiac test or occasional streaks on the outside of the stool.

At the end of two months to ten weeks of treatment, the typical report was, "Lower sigmoid appears almost normal, with rare ulceration. The rectum is slightly injected, and bleeds on rubbing in the lower two inches." The stools at this time were approximately normal. Occasionally constipation occurred. The stools were formed without pus or mucus. An occasional fleck of blood was present on the outside of the stool. The patients' abdominal cramps and rectal urgency had diminished or were absent. They had gained weight and the hemoglobin was high. The diet became less guarded. At the end of the third month of instillations (which were given less frequently) the report was, "Sigmoid appears absolutely normal but for very fine granulation. The rectum is very slightly injected and very finely granular. Two fine pin-point ulcerations were seen in the mid-rectum."

In two patients who had improved, treatment with the preparation was stopped after four months and one teaspoonful of cod-liver oil was given by mouth three times a day. This lapse in therapy coincided with an attack of the grippe in each, and a month later, there was clinical and sigmoidoscopic evidence—stools became blood-tinged and slightly more frequent—which indicated the beginning of a relapse. Treatment was resumed and a similar three to four week period followed before there was unmistakable sigmoidoscopic improvement.

In two other patients, whose treatment was begun at the same time, and continued for months, the improvement has been maintained in spite of intercurrent mild upper respiratory infections.

In several of the patients who apparently responded to therapy, a minimal, residual lesion has persisted in the distal (anal) portion of the rectum, limited to about two inches. This is being treated with the large suppositories of cod-liver oil.

One patient, a mentally retarded, 19 year old boy, with an ileostomy performed a year before in preparation for colectomy, had inanition, moderate drainage from the wound and profuse watery diarrhea. The sphincter control was poor. Some of the difficulty seemed to be psychic, as he showed evidence of a frank schizophrenia. Because of the difficulty of giving him the fluid instillations, the suppositories, at least six per day, were given instead. The ileostomy opening was irrigated with the cod-liver oil emulsion. This patient's colitis improved symptomatically and sigmoidoscopically. Unfortunately his more recent course could not be followed as objectively, because the arthropathy and negative mental attitude combined to make sigmoidoscopy dangerous.

Therapeutic Failures. Two patients failed to respond to this type of

therapy in addition to the previous therapeutic attempts. One was a 15 year old boy, seen through the courtesy of Dr. John Kantor. The patient had the physical development of a 10 year old and had been ill for about four years. There was no clinical improvement at the end of a month of 4-ounce instillations twice daily. There was no sigmoidoscopic follow-up.

Another patient, a 29 year old woman, had four attacks of ulcerative colitis in the course of two years. In the last episode, during which she was hospitalized, she had a septic temperature and X-ray evidence of ulcerative colitis involving practically the entire colon. About 4 ounces of the emulsion were given twice and thrice daily for a period of one month and were retained for only one-half hour, so that the medication could not have reached much beyond the rectosigmoid. The stools became pasty instead of watery, and were guaiac negative for a brief interval. She received numerous transfusions. She developed signs of vitamin B deficiency. A suspicious mass developed in the right lower quadrant. Due to the increasing severity of the clinical course, an ileostomy was performed and the patient died ten days postoperatively. In addition to the acute and chronic non-specific ulcerative colitis, post mortem examination disclosed acute bilateral suppurative pyelonephritis, rheumatic heart disease, and effusions in the pleurae and peritoneum.

Additional Steps in this Therapeutic Study. Other fish liver oils with a greater concentration of vitamins are being used in another group of patients. Then again, in a few patients with the persistent minimal residual lesion, the last two inches of the rectum are being subjected to cold quartz irradiation. In instances where the gravity of the condition demands an operative procedure, such as, ileostomy, appendicostomy, or cecostomy, it is suggested that the operative opening be irrigated with cod-liver oil emulsion. This suggestion is submitted in view of the apparently favorable result obtained in the patient with the ileostomy.

ELECTROCARDIOGRAPHIC CHANGES IN ACUTE NEPHRITIS

ARTHUR M. MASTER, M.D., HARRY L. JAFFE, M.D.,
AND SIMON DACK, M.D.

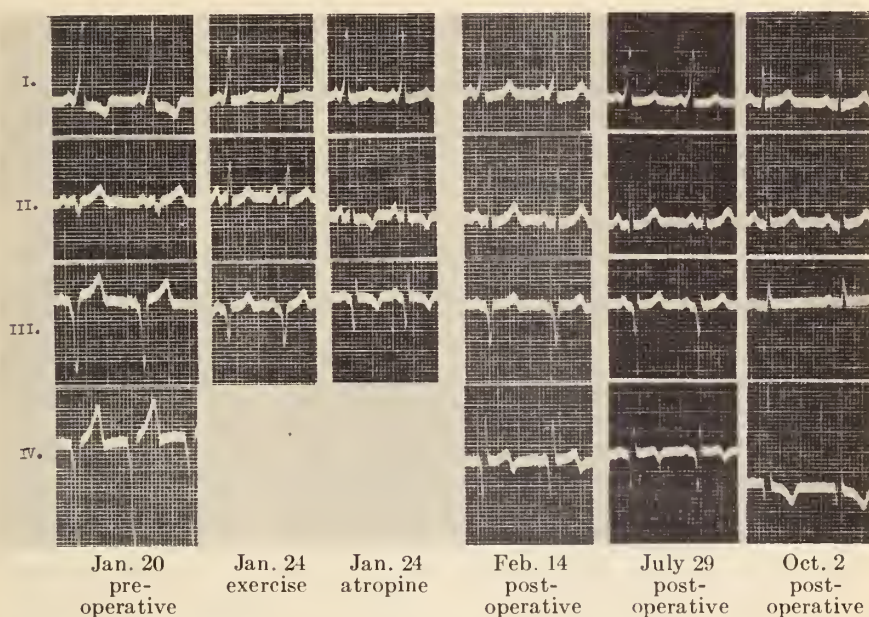[*From the Medical Service of Dr. George Baehr and the
Cardiographic Laboratory*]

For some years we have been impressed by the frequency of cardio-vascular abnormalities in acute nephritis. Not uncommonly the out-standing signs are those of left ventricular insufficiency. It is, therefore, not surprising that definite changes occur in the electrocardiogram, as evidenced by the following case.

History (Adm. 389874). A truck driver, 32 years of age, had had frequent attacks of sinusitis and tonsillitis during the past three years. The last sore throat occurred three weeks prior to admission. Five days later he felt chilly and his temperature rose to 104°F. After several days he complained of severe occipital headache and he vomited. He noticed that his urine had become red.

Physical Examination. The patient presented a puffy, pasty face with slightly edematous conjunctivae. The arteries of the fundus were thin. There was injection of the pharynx and tonsils. The heart was not enlarged, the first apical sound was split and the second aortic accentuated. The blood pressure was 190 systolic and 130 diastolic mm. Hg. The radial arteries were moderately sclerotic. The urine contained three plus albumin, numerous red blood cells and occasional granular casts. The hemoglobin was 68 per cent; the blood chemistry and sedimentation rate were normal. The venous pressure was at the upper limit of normal and the arm-to-tongue circulation time and vital capacity were within average figures. The condition of the patient steadily improved. In a week the blood pressure fell from 190 systolic and 130 diastolic to 100 systolic and 56 diastolic mm. Hg. and then rose to 118 systolic and 82 diastolic mm. Hg. The urine cleared slowly, containing on discharge, however, a moderate amount of albumin, red blood cells and granular casts.

The electrocardiogram on admission showed no abnormality in the standard leads; T-4, however, was upright. Three days later T-1 and T-2 had become inverted, and T-4 diphasic. The very next day T-2 was no longer inverted and T-4 had returned to normal, that is, it was inverted. Within a week T-1 was also upright and later all the T-waves were tall.

Feb. 14   Feb. 17   Feb. 18   Feb. 24   March 2
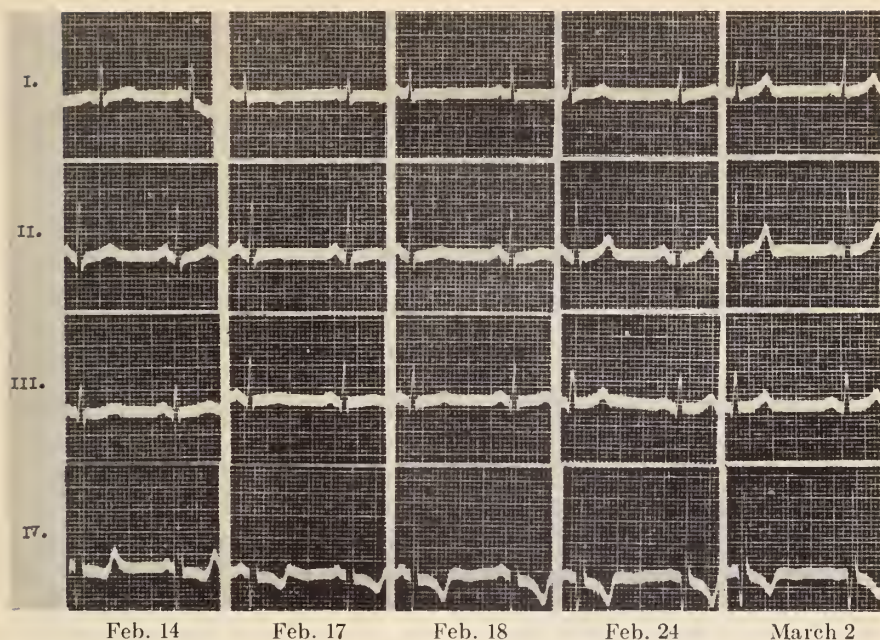
C. S., male, age 32.

February 14, 1936. Regular sinus rhythm, rate 72 beats per minute. T-4 upright, otherwise normal.

February 17, 1936. T-1 and T-2 now inverted and T-4 diphasic.

February 18, 1936. T-1 still slightly inverted, T-2 and T-4 now entirely normal.

February 24, 1936. T-1 now upright.

March 2, 1936. All T-waves moderately tall.

The progressive T-wave changes are definitely indicative of acute myocardial involvement.

DISCUSSION

The progressive changes in the T-waves in the electrocardiogram are definitely indicative of acute myocardial involvement. Because acute nephritis is usually not fatal, there is little pathological material to confirm this. Probably there is widespread damage to the capillaries and arterioles analogous to that in the kidneys. Several authors have reported changes seen with the capillary microscope, but these findings are not universally accepted. In a few cases observed at post mortem in this hospital perivascular lymphocytic infiltration was present in the heart.

ATYPICAL BUNDLE BRANCH BLOCK WITH SHORT P-R INTERVAL IN GRAVES' DISEASE

Effect of Thyroidectomy

ARTHUR M. MASTER, M.D., HARRY L. JAFFE, M.D.,
AND SIMON DACK, M.D.

[*From the Medical Service of Dr. B. S. Oppenheimer and the
Cardiographic Laboratory*]

Wolff, Parkinson and White have reported the occurrence in a small group of normal people of functional bundle branch block with a short P-R interval. They considered this a vagal effect. We have observed a similar condition in a case of Graves' disease without evident myocardial disease. The case is presented because of the changes which occurred in the electrocardiogram after subtotal thyroidectomy.

History (Adm. 388996). A 25 year old housewife, entered the hospital because of typical signs of Graves' disease, including loss of weight, swelling of the neck, prominence of the eyes, nervousness and diarrhea for sixteen months.

Physical Examination. There were definite exophthalmos, moist smooth skin and symmetrical enlargement of the thyroid gland. The heart was not enlarged; the rate was 120 beats per minute, the heart sounds were loud and the pulmonic second sound was accentuated. There was a scratchy systolic murmur at the apex and base. Fluorosopic examination showed slight prominence of the pulmonary conus. The venous pressure was 8 cm. of blood, the arm-to-tongue circulation time, 8.5 seconds. In spite of the definite evidence of advanced Graves' disease, the basal metabolic rate was only plus 18 and, with the administration of iodine, it fell to minus 4. Subtotal thyroidectomy was performed and the patient was discharged in nine days, all her symptoms having disappeared.

Electrocardiographic Study. An electrocardiogram taken before operation (January 20, 1936) showed a regular sinus rhythm, rate about 90 beats per minute. The auriculo-ventricular conduction time, that is, the P-R interval, was shortened to 0.08 to 0.10 second. Marked left ventricular preponderance was present. The QRS complex was of high voltage, slurred, and widened to 0.12 second. In Lead 2 it was small and notched. The R-T segment was depressed in Lead 1 and elevated in the remaining leads. The T-wave was inverted in Lead 1 and upright and tall in Lead 4. In short, a picture of partial bundle branch block was present. In view of the absence of any clinical evidence of myocardial damage in the

patient, and because of reports quoted, the condition was considered functional in nature.

| | Jan. 20 pre- operative | Jan. 24 exercise | Jan. 24 atropine | Feb. 14 post- operative | July 29 post- operative | Oct. 2 post- operative |

D. O., female, age 25.

January 20, 1936. Preoperative record. Regular sinus rhythm, rate 90 beats per minute. P-R interval shortened to 0.08 to 0.10 second. There is marked left ventricular preponderance. The QRS complex is of high voltage, slurred and notched and widened to 0.12 second. QRS small in Lead 2. T-1 inverted, T-4 high and upright. R-T segment depressed in Lead 1, elevated in the remaining leads. Partial bundle branch block.

January 24, 1936. Immediately after exercise. Rate accelerated to 110 to 120 beats per minute, voltage of QRS group becomes normal and the duration reduced to 0.08 to 0.09 second. The P-R interval remains unchanged. The R-T segment and T-waves practically normal in all standard leads.

January 24, 1936. After atropine gr. $\frac{1}{30}$ subcutaneously. Rate increased to 110 to 120. The left ventricular preponderance was lost and a Q-wave appeared in Lead 3, T-1 became upright and T-2 and T-3 inverted. R-T segments normal.

February 14, 1936. Nine days postoperatively. Rate 85. P-R interval measures 0.10 to 0.12 second. Voltage of QRS normal, and duration 0.08 to 0.09 second. T-waves upright in standard leads and diphasic in Lead 4.

July 29, 1936. Similar to previous record, except that T-4 is now almost completely inverted.

October 2, 1936. Eight months postoperative. The electrocardiogram is now entirely normal. The left ventricular preponderance has completely disappeared and the P-R interval measures 0.14 second. The QRS duration is only 0.07 second. The T-waves are normal in all leads.

The effect of several measures was determined. Immediately after exercise the cardiac rate increased to 110 to 120 beats per minute, the

voltage of the QRS group became normal, and its duration reduced to 0.08 to 0.09 second. The P-R interval remained unchanged. The R-T segments and T-waves became practically normal in the standard leads. After injection of $\frac{1}{30}$ grain of atropine sulphate subcutaneously the rate also increased to 110 to 120 beats per minute; the left ventricular preponderance was lost and a Q-wave appeared in Lead 3. The R-T segments became normal. The T-wave became upright in Lead 1 and inverted in Lead 2 and 3. When the heart rate was increased even further by inhalation of amyl nitrite the QRS group duration was actually shortened to 0.06 second.

These striking and immediate changes in the electrocardiogram induced by variations in heart rate and vagal tone were conclusive evidence of the functional and nervous origin of the bundle branch block. It was, therefore, expected that the operation would effect a permanent disappearance of the latter, and, indeed, electrocardiograms since the operation have shown a gradual return of the P-R interval, QRS complex and T-waves to normal in all leads.

It is evident that even so abnormal an electrocardiogram as one showing bundle branch block does not necessarily indicate disease of the heart muscle and may be found in an otherwise normal heart. The mechanism by which this was produced in our case presents interesting considerations. The effect was doubtless mediated through the vagus nerve, since abolition of the action of the latter caused the block to disappear. While Graves' disease is usually considered to be characterized by hyperactivity of the sympathetic nervous system, the entire autonomic system is excessively stimulated. In the case presented presumably the vagus or parasympathetic nerves were more active than the sympathetic.

CLINICAL PATHOLOGICAL CONFERENCES

GEORGE BAEHR, M.D., AND PAUL KLEMPERER, M.D., *presiding*

Wednesday, December 9, 1936

Case I. Subacute Bacterial Endocarditis Complicated by Acute Pericarditis

(From the Medical Service of Dr. B. S. Oppenheimer and the Neurological
Service of Dr. Israel Strauss)

History (Adm. 396485). The patient, a white male of 24, was entirely well
until seven days prior to admission when he began to complain of malaise, con-
stipation, lower anterior inspiratory chest pain, and fever. He had always en-
gaged in strenuous athletic and physical activity without any untoward effects,
in spite of the presence of a long-standing organic cardiac murmur.

Examination. The subject was a well developed, well nourished toxic-appearing
white male. The heart was moderately enlarged and displaced downward. There
were systolic and diastolic murmurs at the apex, a diastolic murmur at the base
and along the left sternal border. The aortic second sound was louder than that
of the pulmonic. Examination of the abdomen presented no abnormalities. There
were neither cutaneous petechiae nor clubbing of the fingers. The most prominent
clinical features on admission were peculiarly neurological, namely, haziness about
the right disc with fullness of the veins, depressed abdominal and cremasteric re-
flexes and hyperactive but equal reflexes in the lower extremities. The tempera-
ture on admission was 103.2°F. The blood count showed 17,400 white blood cells
of which 82 per cent were polymorphonuclear leucocytes, and 3,900,000 red blood
cells. The hemoglobin was 80 per cent. The urine was negative except for an
occasional erythrocyte. The blood urea nitrogen was 14 mgm. per 100 c.c., sedi-
mentation time 12 minutes, venous pressure 10 cm. and blood Wassermann nega-
tive. A chest X-ray examination on admission showed marked left ventricular
enlargement and diffuse aortic dilatation. The electrocardiogram, also taken on
admission, showed an elevated RS-T transition in Leads I, II and III and an
absent Q-4.

Course. The patient ran an extremely stormy course throughout his illness.
The temperature was hectic in type, varying from 98.2° to 106.0°F. Chills re-
curred every two or three days. In view of the neurological findings, the presence
of an acute encephalitis was first suspected. A normal spinal fluid, however,
militated against such a diagnosis. A blood culture positive for streptococcus
viridans revealed the true nature of the illness and the patient was consequently
believed to have a subacute bacterial endocarditis (Streptococcus Viridans) super-
imposed on a rheumatic valvulitis. The clinical course was most unusual for a
case of this kind and was more of the type seen in acute bacterial endocarditis.

Four days following his admission to the hospital the patient developed a loud

scratchy to-and-fro apical precordial friction-rub which was rapidly followed by a pronounced increase in the area of cardiac dullness. A roentgenogram confirmed the clinical impression that the patient had developed a pericardial effusion. At the same time he developed evidence of a moderate left pleural effusion. A pericardial paracentesis yielded 200 c.c. of slightly turbid straw-colored sterile fluid with a specific gravity of 1.016 and a cell count of 2400, 66 per cent of which were lymphocytes. The spleen was not palpable. The only evidence of embolic phenomena was a bluish macular eruption on the lateral portions of the soles of the feet.

Three days before death, the patient's speech suddenly became muffled and indistinct. There were a right central facial palsy, hyperreflexes of the lower extremities with suprapatellar clonus on the right, a right Babinski and absent abdominals. Swallowing also became impaired. He had apparently developed a pseudobulbar syndrome, due to pyramidal tract involvement. Shortly before death, a small amount of fluid was noted at both lung bases. The patient died suddenly five weeks following the onset of his illness.

Necropsy Findings. The pericardial sac was markedly distended with approximately 500 c.c. of a serosanguineous fluid. The opposing pericardial surface presented a typical bread-and-butter appearance. The heart was enlarged and with the pericardium weighed 1150 gm. The cardiac chambers were all moderately dilated; the wall of the left ventricle markedly thickened. The aortic valve was bicuspid in type, thickened and somewhat distorted. Superimposed on it were large masses of opaque, gray, friable vegetations. These extended into the sinus of the right aortic cusp and produced an aneurysmal pocket which progressed anteriorly to involve the epicardial surface at the base of the left ventricle. The left cusp of the aortic valve was partially ulcerated and from it the vegetations extended onto the ventricular surface of the anterior mitral leaflet. The mitral valve showed some slight thickening of the free margin and the associated chordae tendineae. The tricuspid valve was the seat of similar abnormalities. There was also a small vegetation on the subvalvular pulmonic endocardium. Examination of the brain showed a two inch in diameter hemorrhage in the left temporal lobe, edema and some degenerative lesions. The spleen was moderately enlarged, weighing 410 gm., and showed evidence of recent and organized infarcts. The kidneys also presented small infarcted areas.

Microscopically, the myocardium showed a diffuse riddling with so-called Bracht-Wächter lesions. Dr. Klemperer believed the aortic lesion to be of the acquired type, (rheumatic) and that the pericarditis was due to the propagation of the mycotic aneurysm of the aortic sinus onto the epicardial surface.

Dr. Baehr emphasized the very unusual features of the case, namely, the very rapid course (five weeks), the absence of anemia, the septic type of temperature and the development of an acute pericarditis. Libman has pointed out that acute pericarditis is rare in subacute bacterial endocarditis in contrast with rheumatic endocarditis. We have now observed acute pericarditis three times in subacute bacterial endocarditis and in each instance the infection of the pericardium resulted, as in this instance, from the penetration of a mycotic aneurysm of the sinus of Valsalva.

Reported by HENRY HORN, M.D.

Case II. Prostatic Abscess Secondary to a Furuncle of the Back; Suppurative Thrombophlebitis of the Prostatic Plexus; Staphylococcus Aureus Bacteremia; Coarse Nodular Cirrhosis of the Liver

(From the Surgical Service of Dr. Edwin Beer)

History (Adm. 396426). The patient, an acutely ill 48 year old white male, was hospitalized because he had had repeated chills for two days and some burning on urination for 18 hours. The patient's previous history included anti-syphilitic therapy about 1916 and an associated gonorrheal urethritis. In 1918 he was jaundiced for a period of five weeks. In 1932 a large palpable spleen with a thick firm edge was discovered, the cause of which could not be determined. There was no associated hepatomegaly at this time and blood examinations were not significant. In 1934, he was operated upon for what was probably a stricture of the urethra with an accompanying prostatitis (performed at another hospital). Eight days before admission, the patient presented himself with a small furuncle in the mid-back, which was conservatively treated with wet dressings. Four days after the appearance of the furuncle he began to have fever and two days thereafter chills began to occur.

Examination. The patient was acutely ill; temperature 103°F., pulse 108, respirations 26 per minute. The spleen was palpable. A large, boggy, tender left prostatic lobe was felt by rectum. The urine contained numerous pus cells and gram-positive cocci and a slight massage of the prostate produced moderately profuse urethral bleeding. Blood culture was positive for staphylococcus aureus.

Course. On the day following his admission the patient began to complain of severe generalized muscular pains and developed several indurated exquisitely tender areas on various parts of the body, which were considered by Dr. Beck to be embolic in nature. There were also numerous cutaneous emboli which subsequently broke down to form small pustules. Within 24 hours of admission a loud friction-rub developed over the cardiac area and signs of basal bronchopenumonia appeared. Six to eight hours later a pericardial effusion developed coincident with the disappearance of the friction rub. The pneumonic process spread rapidly, death occurring eight days after onset of his illness. By the time of his demise the furuncle had entirely healed.

Necropsy Findings. The prostate was soft, slightly increased in size and on section presented many small abscesses. The veins comprising the prostatic plexus were filled with purplish red ante-mortem thrombi. There were multiple metastatic pulmonary and renal abscesses, acute fibrino-purulent pericarditis and acute fibrinous pleuritis. A very significant and interesting incidental finding was a coarse nodular (toxic) cirrhosis with splenomegaly (800 gm.) (See accompanying figure).

Comment. Dr. Beck was of the opinion that the furuncle of the back had produced a transient bacteremia with lodgement of bacteria within the prostate gland, the previously diseased prostate constituting a *locus minoris resistentiae*. The prostatic abscess subsequently involved the prostatic venous plexus and resulted in the recurrence of a persistent septicemia. Dr. Baehr agreed with this pathogenetic concept and compared such a train of events with those encountered in the development of renal abscesses with involvement of a renal vein and second-

ary hematogenous distribution of the bacteria.   These renal abscesses with secondary hematogenous dissemination of staphylococci usually produce their first clinical manifestation about two weeks after the occurrence of the furuncle of the skin from which the primary transitory bacteremia occurred.

The pathological findings, Dr. Klemperer felt, confirmed the clinical opinions in view of the presence of abscesses not within the acini which ordinarily occurs in a primary type of infection but rather within the stroma of the gland.   This, he felt, was unequivocal evidence of a hematogenous dissemination.   The presence of staphylococcus aureus as the causative organism also seemed to favor this view.   Evidence of septicemia pathologically was offered by the multiple ab-

Coarse nodular cirrhosis of the liver

scesses in the lung, kidneys, and a purulent pericarditis.   The latter arose from the rupture of a purulent myocardial focus into the epicardium.

The cirrhosis of the liver with the associated splenomegaly was held to be toxic in origin, representing perhaps the end result of a so-called catarrhal jaundice. The rapid complete healing of the majority of instances of catarrhal jaundice, however, was emphasized.   Two examples of such complete healing of clinically typical catarrhal jaundice were recalled by Dr. Klemperer which had later succumbed to an intercurrent disease several months after the subsidence of the jaundice.   The livers of these subjects were perfectly normal upon microscopic study.

Reported by HENRY HORN, M.D.

Wednesday, January 27, 1937

Case I. Terminal Ileitis.   Rheumatic Heart Disease

(From the Surgical Service of Dr. Richard Lewisohn and Medical Service of
Dr. George Baehr)

History (Adm. 402372).   The patient, a white female, aged 17, was first admitted to the gynecological service of The Mount Sinai Hospital in July 1936 with a six weeks' complaint of postprandial lower abdominal pain and vulvar swelling. There was a history of chorea at the age of five with five annual recurrences thereafter, but no history of cardiac embarrassment.   Examination at that time revealed a moderate degree of left cardiac enlargement, a presystolic crescendo murmur, snapping first apical sound and a soft diastolic apical murmur.   The blood pressure was 118 systolic and 60 diastolic.   A round resistant mass was palpable in the right lower quadrant.   On vaginal examination the uterus was found to be normal, but to its right was found a cystic, tangerine-sized mass.   Occupying a semicircular area to the left of the anus was a reddened, non-tender, edematous, coxcomb-like excrescence made up of three distinct lobules.   The right labium majus was twice the size of the left and appeared edematous.   The Frei and blood Wassermann reactions were negative.   Abdominal exploration disclosed a right dermoid cyst which was resected with the right ovary.   The terminal 4 inches of ileum, the cecum and appendix were found enlarged, their walls thickened and hemorrhagically discolored.   A few discrete lymph nodes were found in the adjacent mesentery, one of which was excised for microscopic study and proved to be the seat of a non-specific hyperplasia.

The patient was then transferred to the medical service for further study.   A barium enema revealed a stenosing lesion of the terminal 6 inches of ileum and a marked irregular stenosis of the caput coli suggestive of regional ileitis.   Agglutination for dysentery was negative.   A Rehfuss test meal showed free acid up to 20. A second exploratory laparotomy was then performed.   The terminal 6 inches of the ileum presented an inflammatory lesion.   Two points, one 3 inches from the ileo-cecal angle and the other approximately 6 inches from the angle, were more extensively involved.   Here the induration, redness and narrowing were most severe.   The cecum was adherent to the abdominal scar and omentum and therefore could not be visualized.   Ileosigmoidostomy with exclusion of the inflamed portion of the intestinal tract was accomplished.   Except for the development of a pneumonic process over the left chest posteriorly, the postoperative course was uneventful and the patient was discharged to the Out-Patient Department on the fourteenth postoperative day, forty days after admission.

Second Admission.   The patient was readmitted December 16, 1936, approximately four months after her last operation, with a history of occasional right-sided abdominal pain and a recent increase in the number of daily stools.

Examination.   The additional pertinent physical findings were an irregular, slightly tender mass within the right lower quadrant, enlargement of the right labium majus and a firm perianal mass 1.5 by 0.75 inches.   The urea nitrogen was 12 mgm.; CO_2, 54.5 vol. per cent; blood chlorides 585 mgm. per 100 c.c.   The blood Wassermann reaction was negative.

Course.   Resection of the distal ileum, cecum, ascending colon was performed with closure of fistulous communications between the ileum and transverse colon

and between a high loop of ileum and a portion of the non-functioning ileum. Several hours after this operation the patient's respirations increased to 32 per minute and numerous fine basal râles were heard. On the morning following operation, the respiratory rate had risen to 40 per minute. A moderate degree of cyanosis of the lips and nail beds also appeared. A roentgenogram of the chest showed evidence of an extensive bronchopneumonia. The patient's condition rapidly grew worse, her cyanosis increased in intensity, pulse mounted to 150–170 and became very poor in quality. Her temperature rose to 103.4°F., death occurring approximately twenty-four hours following her second operation.

Anatomical Findings. Surgical specimen consisted of 24 cm. of ileum, appendix and 10 cm. of cecum and ascending colon. The serosal surface of the ileum was smooth and injected. The mucosa of the proximal 11 cm. of ileum was granular and congested; that of the distal 13 cm. of ileum, pale and superficially scarred. The wall of this portion gradually increased in thickness to 5 mm. toward the ileocecal valve. The mucosa over the ileocecal valve was deeply scarred. Projecting from this area was a cherry-sized, polypoid, pedunculated mucosal polyp. The mucosa of the cecum and ascending colon was pale, flat and the seat of shallow scars and three scattered small pedunculated polyps. Several small shallow ulcers were also noted in the mucosa of the transverse colon. The appendix measured 15 cm. The mucosa in its proximal 4 cm. was granular, edematous, hemorrhagic and ulcerated. Many flat, stellate, hemorrhagically ulcerated areas were also found toward the tip. The heart was moderately enlarged for the size of the individual and weighed 240 gm. There was evidence of a chronic rheumatic interstitial valvulitis of the mitral and aortic valves with a recently superimposed verrucous endocarditis of the mitral and tricuspid valves. The lungs were markedly edematous and congested. There were also chronic passive congestion of the spleen and kidneys, a moderate amount (1000 c.c.) of fluid in the peritoneal cavity, a few focal mucosal ulcerations of the transverse colon and the perianal inflammatory zones as described clinically.

Comment. Although the endocarditis found at necropsy was overshadowed clinically by the abdominal complication, Dr. Klemperer felt that the cardiac lesion was primarily responsible for the cardiac failure and the patient's death. The anal lesions were described as fibrotic and not epithelial in type and therefore were not condylomata. The diarrhea of which this patient complained may have been the cause of inflammation of the corium and its subsequent thickening.

In discussing the surgical procedures in use for this disease, Dr. Crohn alluded to two cases operated upon by Dr. Lewisohn in which a simple short-circuiting operation led to complete healing of the regional inflammatory process. Here a complete diversion of the intestinal current was effected by transection of the ileum and coincidentally performed ileosigmoidostomy. On the basis of this experience Dr. Crohn felt that the side-tracking procedure might ultimately prove to be all that is necessary to effect relief and, probably, cure in terminal ileitis.

Case II. Benign Adenoma of the Bronchus

History (Adm. 402041). The patient, a white female aged 71, first entered The Mount Sinai Hospital in 1926, complaining of fever and an unproductive cough of six days' duration. Her previous history disclosed bronchopneumonia in 1921, pleurisy in 1924 and essential hypertension for nine years. Examination at this

time revealed signs of a bronchopneumonia of the right lower lobe.   Fever persisted for six weeks with afternoon rises to 102–103°F. and then gradual defervescence.

The patient was readmitted in 1928 with a history of recurrence of broncho-pneumonia in March of 1927 and the complaint of fever, slight productive cough for three days and sharp pain beneath the right scapula on deep inspiration.   Consolidation of the right lower lobe with signs of a moderate amount of fluid were found.   The chest X-ray examination revealed a chronic pneumonitis with pleural thickening.   Temperature fell by lysis after two weeks and the patient left, improved.

In 1929 and 1930 she experienced similar pulmonic flare-ups with expectoration of blood-streaked sputum.   The patient was then looked upon as a case of chronic bronchitis, bronchiectasis and pneumonitis.   She was readmitted to The Mount Sinai Hospital in May 1931 because of the hemoptysis and a slight productive
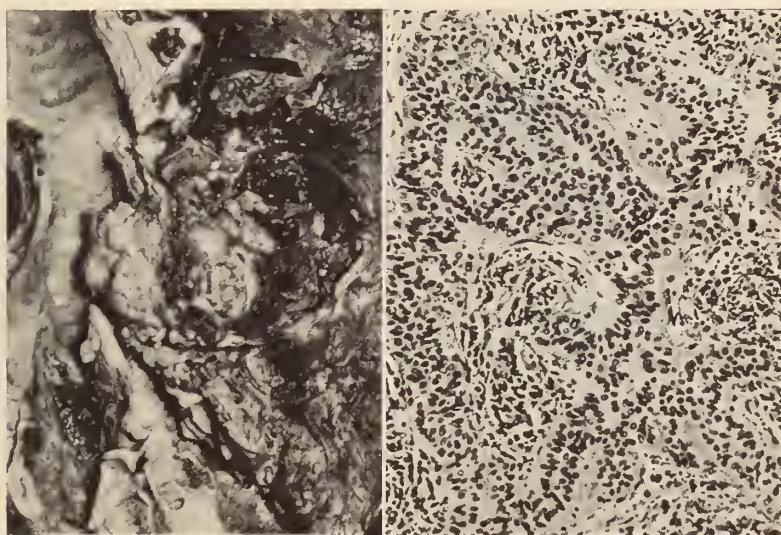
Polypoid adenoma of right lower bronchus with extension through bronchial wall and into adjacent bronchiectatic cavity

cough.   Examination of the chest showed dulness at both bases, more marked on the right, with coarse rhonchi throughout the right chest and many crackling râles over the left lower lobe.   Repeated sputum examinations for tubercle bacilli were negative.   In view of the recurrent hemoptysis, the possibility of bronchial neoplasm was suggested by Dr. Wessler.   Bronchoscopy was therefore performed. On the posterior wall of the right bronchus opposite the level of the middle lobe bronchus was noted a rounded mass which almost completely occluded the bronchial lumen.   A considerable amount of thick pus was observed distal to the obstruction.   A biopsy of this mass was reported as a fibro-epithelial polyp.   The reason for the recurrent attacks of pneumonitis and hemoptysis now appeared to be clear.   One month later, bronchoscopic examination presented granulation at the former site of the tumor with a small quantity of secretion in the right lower lobe bronchus, distal to the growth.   Soon thereafter the right lower lobe bronchus

was found completely occluded by tumor, a section of which was removed and reported as a basal cell epithelioma. Radon seeds were then implanted into the tumor site and removed ten days later. An X-ray examination of the chest before discharge showed a pronounced diminution in the pneumonic infiltration of the right lower lobe.

The patient was again bronchoscoped in October 1931. A small, soft, nodular, readily bleeding growth was again found on the lateral and posterior walls of the right lower lobe bronchus below the posterior division, 6 mm. in width. A specimen was removed and the remainder treated with diathermy.

Bronchoscopic examination in December of 1931 revealed no evidence of tumor growth. The patient continued in good health until October 1932 when she developed dysuria, frequency, polyuria and pyuria. She was treated by boric acid and argyrol irrigations with some improvement. Early in March 1933 she again developed fever, chilliness and weakness. Marked dulness, coarse râles and bronchial breathing were detected over the right lower lobe posteriorly. Bronchoscopy this time showed a tumor recurrence, a biopsy of which revealed a basal cell epithelioma similar in morphology to that previously reported. In January of 1934 a course of deep X-ray therapy was instituted over the right lower lobe. A chest X-ray examination now showed a dense, homogeneous shadow situated at the site of the root of the right lung and a similar shadow at the root of the left lung. These were interpreted as representing metastatic carcinoma of the tracheobronchial lymph nodes.

In 1934 the patient's blood pressure became more elevated, the systolic ranging between 170–180, and the diastolic between 90–98. Anginal seizures appeared consisting of precordial pain with radiation down the left arm which were associated with moderate dyspnea. In November, 1936, one month preceding her last admission to the hospital she suffered with many recurrent attacks of precordial pain, and on the day before admission the patient had an unusually severe attack of precordial pain. Signs of shock supervened and her blood pressure fell to 80 systolic and 44 diastolic. Death occurred four days after hospitalization.

Necropsy Findings. The lungs were somewhat enlarged except for a shrunken right lower lobe. The pleura over the right lower lobe was densely thickened, while over the upper two lobes scattered fibrous tags were noted. The right lower lobe throughout was non-crepitant. Approximately 1 cm. below the origin of the eparterial branch of the right lower lobe bronchus a dense, firm, white nodular mass was encountered. This tumor occupied the posterior lateral wall of the right main bronchus and almost completely occluded its lumen. It extended along the lateral wall of the anterolateral bronchus of the right lower lobe for a distance of about 2 cm.; then laterally and posteriorly through the bronchial wall for a distance of about 2 cm. outside the wall of the right main bronchus, resting apparently within an enlarged bronchiectatic cavity. The bronchus distal to the tumor mass was dilated and filled with thick, greenish, mucopurulent material. The right lower lobe presented numerous bronchiectatic cavities separated by firm, non-crepitant islands of lung parenchyma. The left lung presented a moderate degree of emphysema and edema. The heart was moderately enlarged and chambers dilated. The myocardium of the anterior wall, posterior wall and anterior two-thirds of the septum of the left ventricle and portions of the right ventricular wall was the seat of extensive recent myomalacia. Organized and recanalized thrombi were

found in the right coronary, circumflex and anterior descending branches of the left coronary artery. There was also a marked arteriosclerotic narrowing of the posterior interventricular branch of the right coronary artery. The anatomical cause of death was the extensive myocardial infarction.

Comment. In view of the long-standing clinical history and removal of the tumor during bronchoscopy, Dr. Baehr brought up the question as to whether the original tumor, which may have existed since 1921, was a carcinoma or a benign neoplasm. Dr. Klemperer described the peculiar combination of fibrous tissue and epithelial cells at the time of the first biopsy in 1931. The cells, he pointed out, did not resemble those usually found in an adenoma, but were more of the basal cell variety. At the time of the second bronchoscopic biopsy a month later he reported the neoplasm to be a basal cell epithelioma.

In regard to recurrence and growth of these tumors, Dr. Klemperer recalled several instances characterized by a purely local expansive type of growth. In one such case the entire lung was found involved. In spite of the extensive tumor growth in this case and the seventeen year clinical history, no metastatic foci were discernible. The histologic picture of this tumor was similar to that of the present case. Still another case was a local basal cell epithelioma of a bronchus with a nine year course. Because of the absence of metastases Dr. Klemperer felt that the lesion was a benign epithelioma rather than a true carcinoma.

Case III. Acute Hemorrhagic Pancreatitis; Hematoma of the Duodenum

(From the Surgical Service of Dr. Edwin Beer)

History (Adm. 399009). The patient, a 30 year old white male, was admitted to the hospital because of upper abdominal pain, nausea and persistent vomiting for one day. These symptoms had followed alcoholic excesses. The pain steadily increased in intensity to the time of admission and remained most marked in the upper abdomen just above the umbilicus. His previous history was essentially negative except for a right orchidectomy (for tumor?) in May, 1936 at another hospital.

Examination. The patient was an obese, acutely ill male. The temperature was 99°F., pulse 90 and respirations 20 per minute. There was moderate tenderness to pressure without rebound tenderness in the right and left upper abdominol quadrants. Examination of the heart, lungs and rectum was not significant. Urinalysis showed a trace of albumin, glucose 1.5 per cent and acetone four plus.

Dr. Baehr considered this degree of acetonuria and glycosuria of significance in view of the fact that the patient had been vomiting for only one day. He expressed the opinion that this finding should have suggested the possibility of acute pancreatic disease and that an examination of the blood for amylase would have supplied confirmatory evidence.

The icteric index was four, Van den Bergh direct-negative; indirect 1:250,000, bilirubin 0.4 mgm. The blood urea nitrogen was 18 mgm., blood sugar 280 mgm., cholesterol 310, and cholesterol ester 35 per 100 cc. The blood Wassermann was negative.

Course. The patient continued to vomit a blackish-brown material which later became coffee-ground and gave a four plus guaiac reaction. Tenderness persisted in the right upper quadrant and was associated with an increased diffuse abdominal resistance. His temperature rose to 103.6°F. within twelve hours of admission.

An exploratory laparotomy disclosed scattered areas of fat necrosis in the omentum and in the retroperitoneal tissue. A large mass was palpated in the region of the head of the pancreas which also involved the second portion of the duodenum. The patient reacted badly during the operation, his pulse became thready, respirations labored and cyanosis appeared. Death occurred four hours following the laparotomy.

Necropsy Findings. The pancreas was enlarged to approximately three times its normal size. The peripancreatic fat showed numerous pea-sized chalky areas. The head of the pancreas and second portion of the duodenum were covered over by bloody material. The tissue in the region of the head of the pancreas was soft and flabby, purplish-grey with numerous hemorrhagic zones. The remainder of the organ showed a scattering of hemorrhages with a few soft, grey and hemorrhagic structureless areas. The pancreatic duct was slightly dilated and opened anomalously into the common bile duct about 1 cm. from the tip of the Ampulla of Vater. The duodenal wall was irregularly thickened, varying from 0.5 cm. to 7.5 cm. due to the mural dissection by friable blood clot and the periduodenal tissue presented a similar infiltration. This hemorrhage had produced marked narrowing of the duodenal lumen and at a point opposite the ampulla, the diameter was but 1.5 cm. The hemorrhagic infiltration extended through the upper three inches of jejunum. There were hemoperitoneum (250 cc.), hemopericardium (25 cc.), a right hemothorax (200 cc.) and scattered hemorrhages into the lungs.

Comment. Dr. Klemperer felt that the pathological findings corresponded to those originally referred to as pancreatic apoplexy. The associated necrosis of the pancreas was formerly attributed to the hemorrhage. The point was emphasized, however, that hemorrhage is merely incidental to blood vessel erosion produced by necrosis. The general factors which may play a rôle in the production of pancreatic necrosis (hemorrhagic pancreatitis) were then reviewed—namely, bile reflux in the pancreatic duct, duct spasm, vascular lesions with secondary ischemic necrosis, hematogenous or ascending infectious processes, obstruction by calculi of the larger or by epithelial metaplasia of the smaller pancreatic ducts and pressure by neoplasms.

Dr. Baehr felt that the high intestinal obstruction produced by the hematoma of the duodenal wall was an important contributory factor in the death of this patient. The early death was probably due to an alkalosis, resulting from the high intestinal obstruction. If this had been suspected and confirmed by analyses of the blood for chlorides, CO_2 combining power and total nitrogen, adequate quantities of hypertonic saline might have tided the patient over the critical period. The subsequent formation of localized abscesses might then have been drained surgically. In his experience patients operated upon in the early stages of a severe acute pancreatitis usually die. Neither the peritoneum nor the entire pancreas can be drained. If the patient can be tided over his shock, alkalosis or ketosis, etc. and live to develop a localized abscess, this can then be drained successfully.

Reported by HENRY HORN, M.D.

Ernst Rosenfeld

February 17, 1880–June 13, 1937

Death, sudden and unfailing in its impartiality, has taken our good friend, Ernst Rosenfeld, from our midst.

The fatal blow fell upon him when still so full of vigor and determination to work for The Mount Sinai Hospital, which was so dear to him.

To him The Mount Sinai Hospital meant so much more than a cluster of impressive buildings and marble stairways. To him it was a sacred place where man should give, without stint, his best to his fellow man.

Courteous, kind and with an inherent sense of dignity in his dealings with all, he never failed to show his admiration for the "doctor," though, at times, it was mixed with well meant, and not undeserved, criticism.

His eyes, however, were fixed, above all, upon the men in the lower ranks of the medical and surgical staffs, and, particularly, upon those whose work was mainly in the Out-Patient Department. Welcome were his regular and frequent visits to the "dispensary." His pleasant and solicitous, but none the less search in and earnest inquiries into the needs of the doctor, patient and employee well showed where his sympathies lay. They were with the men and women, still young in their efforts to make their way. Their desires and their wants he had close to his heart, and their disappointments he felt as keenly as his own. They, like so many others, well knew that no appeal to him would go unanswered and no just cause— unchampioned.

Thus, deep and sincere will remain the sense of our loss and long will his cherished memory live in our hearts.

JOSEPH H. GLOBUS.

ABSTRACTS

Members of the hospital staff and the out-patient department of The Mount Sinai Hospital are invited to submit for publication in this column brief abstracts of their articles appearing in other journals.

Theca Cell Tumors. S. H. Geist. Am. J. Obst. & Gynec. 30: 480, October 1935.

A group of five tumors is described. They are composed of two distinct elements, fibrous tissue and epithelioid cells. The latter histologically resemble the cells of the theca interna. Fat tissue is also present. These tumors either store or produce an estrogenic substance and are associated with a definite clinical picture. They usually occur in women at or past the menopause with atypical bleeding.

Because of the histologic, chemical and biological resemblance of these tumor cells to the theca interna cells of the ovarian parenchyma, it is suggested that the forerunners of the theca interna cells in the ovary probably constitute the basis of the tumor formation. They are apparently benign.

The Use of Coley's Mixed Toxins in Ophthalmology. Further Observations. J. Levine. Arch. Ophth. 14: 554, October 1935.

The present report is a study of the use of Coley's mixed toxins as a foreign protein in fever therapy. It was found that on the average three minims injected intramuscularly were sufficient to give a rise of temperature to 103°F., coming on invariably six hours after the injection. This therapy is advised for ocular conditions such as iritis, iridocyclitis, kerato-iritis, secondary glaucoma, uveitis, sympathetic ophthalmia, etc.

Tuberous Sclerosis in the Infant. J. H. Globus and H. Selinsky. Am. J. Dis. Child 50: 954, October 1935.

The typical triad of symptoms characteristic of tuberous sclerosis, viz., convulsive seizures, retarded or arrested mental development and adenoma sebaceum, lead to the clinical diagnosis when they are present. But in most cases, especially in infants, this triad is incomplete. The occurrence of this disease in infancy is recorded very infrequently; the two cases reported by the authors were four months and five months old, respectively. In both instances, convulsive seizures were the predominating symptom.

The gross pathologic features consisted of convolutional areas which were harder to the touch (sclerosed), flattened and widened. Ependymal granulations were present. On histopathologic study, the following features were striking: (1) lack of normal architecture with disordered cellular arrangement in the tuberous zones, (2) dense glial proliferation, (3) presence of cell anomalies, e.g., giant glia cells and monstrous ganglion cells, (4) presence of areas which have the character of true tumor formation, (5) aggregations of microglia in the ependymal granulations.

Two opposing concepts of the disease are held. According to one, it is an expres-

sion of disordered development, whereas the other theory considers the disease to be a primary neoplastic process of the glial apparatus.

Finally, it is suggested that, although the clinical findings in infants are too meagre to permit certain recognition, one may suspect the presence of the disease in cases where convulsive seizures and arrested mental development are manifested, particularly in association with blindness or maldevelopment or tumor formation in some other part of the body.

Histogenesis of Certain Ovarian Tumors and Their Biologic Effects. S. H. Geist. Am. J. Obst. & Gynec., 30: 650, November 1935.

Four groups of tumors are described. (1) Granulosa cell tumors arising from unused granulosa cell fore-runners. (2) Theca cell tumors arising from theca interna cell fore-runners. Both types store or produce an oestrogenic hormone and both types affect the host by exaggerating certain aspects of the female physiology. There are histogenic and clinical points of difference, however. (3) Rete cell tumors or arrhenoblastoma arising from male directed elements in the ovary. These affect the host by causing a defeminization with the development of male type hair, male gait, voice and larynx. The loss of female breast contour, the loss of menstruation and the atrophy of the genitalia also occur. (4) Neuter cell tumors or dysgerminoma have no incretory function and no pathologic physiologic effect on the host. They occur in younger individuals often with defective gonads and atypical somatic development.

Acute Cholcystitis Associated with Pancreatic Reflux. R. Colp, I. E. Gerber, and H. Doubilet. Ann. Surg., 103: 67, January 1936.

In a certain number of cases in the human, the anatomic relationship allows the ductus choledochus and the duct of Wirsung to be converted into a single continuous channel by obstruction of the papilla of Vater. This obstruction might be caused either by a calculus, or by edema of the duodenum and papilla, or by spasm of the sphincter of Oddi muscle.

Once a single channel has been established, bile may flow into the duct of Wirsung or pancreatic juice may flow into the choledochus. The direction of the flow probably depends upon the relative pressure in each duct.

If pancreatic juice refluxly enters in the biliary system, no clinically recognized sequelae may result. On the other hand, if the pancreatic ferments are present in the gall-bladder bile in sufficient concentration and amounts to change its usual acid reaction to alkaline, the bile salts may act destructively on the gall-bladder wall together with the activated pancreatic ferments. As a result of the chemical inflammation caused by these various factors, either an acute cholecystitis or non-perforative biliary peritonitis may result.

Three cases are reported of acute cholecystitis in which the gall-bladder bile was alkaline and contained large amounts of pancreatic ferments.

Cystic Disease of the Lung. H. Hennell. Arch. Int. Med. 57: 1, January 1936.

Eight cases of cystic disease of the lung are described illustrating the clinical features, the diagnosis and the therapeutic problems of the condition. The pneumodynamics of air cysts of the lung are analyzed in considerable detail including such features as the mechanism of their development, persistence, growth to giant size, spontaneous disappearance, etc. The various types of air cysts of the lung are described and the therapeutic procedures applicable in their treatment are discussed.

Lesions in the Auriculoventricular Conduction System Occurring in Rheumatic Fever. L. Gross and B. M. Fried. Am. J. Path. 12: 31, January 1936.

One hundred and ten human hearts have been examined in order to determine the

nature and frequency of the lesions occurring in the Tawara node and bundle of His in rheumatic fever. Sixty of these cases represent active rheumatic fever, 25 cases inactive rheumatic fever, and 25 cases non-rheumatic material. It has been shown that in active rheumatic fever there occurs a variety of inflammatory and vascular phenomena within the horizontal conduction system as well as in the surrounding tissue. Even when studied in a few representative specimens from each bundle, the incidence of these lesions was approximately 66 per cent in the active material. It is probable that a study of more sections would have indicated a higher incidence. Very few of these lesions are of a specific or highly characteristic nature. The inactive rheumatic cases showed few pathological changes. This is in keeping with the functional differences observed between these two groups. Attention has been called to the high incidence of inflammatory lesions in the collagenous extension of the septum fibrosum and a discussion of the possible mechanisms concerned with the spread of the rheumatic infection to the bundle tissue is given. A description of the topographical relations of the horizontal conduction system in the human heart, together with the findings in 25 non-rheumatic control cases, is also given.

Syphilis of the Bladder. E. O. FINESTONE. Surg., Gynec., & Obst. 62: 93, January 1936.

In the past fifteen years there has been no comprehensive review of the subject of syphilis of the bladder. The literature since 1900 was carefully reviewed and 159 cases selected for analysis. About 50 others were not included in the series because they appeared in unobtainable foreign periodicals or were virtually duplicated in certain publications. The incidence of syphilis of the bladder seems to be very much less in this country than abroad, and this is probably dependent on the marked laxity in the reporting of cases which are neither thoroughly studied nor adequately controlled. Of the 158 reported cases, in only 8 were the lesions subjected to microscopic study. Of these, one showed typical histopathology; two are claimed to have shown specific histopathology, but are not reported in detail and the five others gave descriptions of non-specific inflammation.

The diagnostic criteria used were: (1) history of syphilis, (2) presence of luetic lesions, (3) positive blood Wassermann, (4) cystoscopic appearance, (5) response to antiluetic treatment with disappearance of the lesions cystoscopically. Most of the cases presented a few of these criteria, and only the minority of the cases presented every one of the diagnostic criteria. Two cases, one of which possesses all these diagnostic criteria, are described in detail, demonstrating the pitfalls which are encountered in the presence of bladder disease and concomitant syphilis.

Not one of the cases described measures up to the standard set by Young, who maintains that the spirochaeta must be demonstrated in the lesions.

The Effect of Calcium Injections on the Human Heart. K. BERLINER. Am. J. M. Sc. 191: 117, January 1936.

Intravenous calcium injections are dangerous to the heart when administered rapidly. In 26 normal individuals, rapid intravenous injection of 10 cc. of a 20 per cent calcium gluconate solution produced marked electrocardiographic changes. These changes consisted in flattening or inversion of the T-waves in 92 per cent of the cases, flattening or inversion of the P-waves in 54 per cent, and a marked bradycardia in 67 per cent. Besides, ventricular premature beats, sinus arrhythmia, and even sinus arrest accompanied by syncope were occasionally observed. Intravenous injections of 10 per cent of physiological salt solution given as controls to 18 normal individuals had no effect whatsoever on the electrocardiogram.

In this investigation, for the first time, experimental proof has been supplied of the direct effect of calcium upon the normal human myocardium.

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CONTENTS

CONGENITAL ANEMIA OF THE NEWBORN

A Case Report

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[From the Pediatric Service of Dr. Bela Schick]

This case, typical of congenital anemia, presents the opportunity for a brief discussion of the condition and its relationship to other forms of anemia of the newborn. Therapeutically it is important because of the dramatic reaction to a single transfusion.

History (M.M. Adm. 393952). A two weeks old female of Jewish parentage was admitted to the pediatric service of Dr. Bela Schick because of increasing pallor and icterus. The hemoglobin taken a day prior to admission had been reported as 26 per cent. The patient, a second child, was delivered at full term spontaneously. The birth weight was six pounds, six ounces. There was no history or evidence of birth trauma. The child was breast fed and also had been receiving supplementary feedings of cow's milk. No cod liver oil, orange juice, or vitamin concentrates had been given, nor was any medication administered. On the third day after birth, the baby's skin appeared slightly icteric. The icterus faded and the color seemed perfectly normal until the tenth day. At this time jaundice reappeared and, in addition, there was a noticeable pallor. Icterus and pallor concomitantly became progressively more severe up to the time of admission. With the onset of jaundice, the appetite diminished and the child took the feedings poorly. There was no elevation of temperature, no diarrhea, cough or evidence of infection. Urine appeared normal in color, and the stools were of normal appearance, never tarry, bloody or clay colored.

There was no familial history of lues, tuberculosis or blood dyscrasia. However, among several members of the mother's family there was congenital deafness and the mother herself was afflicted with deafness of mild degree. She had had two pregnancies. The first child, born at full term, died at the age of one week, following operation for harelip. The second pregnancy was entirely uneventful and uncomplicated, ending at term in a normal spontaneous delivery of this patient. On the tenth day post partum the mother developed caked breasts and a temperature of 104°F. This complication lasted two days, subsiding spontaneously. The infant's breast feedings were not discontinued at this time.

Examination. The infant was extremely pale but did not appear acutely ill. Movements were vigorous and the patient had a lusty cry. The general nutrition seemed good. The skin, aside from the marked pallor, had a slight icteric tinge. This was also evident in the sclerae. No petechiae or ecchymoses were seen. The liver edge was felt 2 cm. below the costal margin. The spleen was not palpable at this time. The remainder of the examination revealed no abnormalities.

Two hours after admission a blood transfusion, consisting of 85 c.c. whole citrated blood, was given. The father was the donor—group II; Kahn test was negative. Improvement was almost instantaneous. The skin took on a pinkish hue, and the appearance of jaundice was gone the following day. The spleen at this time became palpable 1 cm. below the costal margin and remained so until discharge. Following the transfusion no other therapy was employed. The infant was kept on a diet consisting of breast milk formulas, which it took very well. Improvement was steady and by the sixth day of its hospital stay the general condition was so good that the child was discharged.

The child's progress, thereafter, has been satisfactory. At five months of age she weighed 16 pounds, 2 ounces; liver and spleen were not palpable, mucous membranes appeared pink and her general condition was excellent.

Laboratory Data. *June 2, 1936:* Icteric Index 38; Van den Bergh direct, negative; indirect, positive 1:25,000; serum bilirubin 4.0 mgm. per cent; bleeding time, $2\frac{1}{2}$ minutes; coagulation time, 5 minutes. Hemolysis began at 0.44 and was complete at 0.24 identical with reaction of a

BLOOD FINDINGS	6/1/36*	6/2/36	6/3/36†	6/5/36	6/8/36
Red blood cells.......	1.34 M.	1.45 M.	3 5 M.	3 5 M.	
Hemoglobin (Sahli)...	26%	28%	62%	70%	77%
Grams per 100 c.c...		4 5	10	11 2	12.3
Color index..........	0 97	0 97	0 89	1.0	
White blood cells‡....	29,050	18,900			
Polymorphonuclear.	52%	34 5%	60%	49%	
Segmented..........	36%	6 5%	48%	37%	
Non-segmented.....	16%	28 5%	12%	12%	
Myelocytes...........	4%	1 0%	1%	1%	
Eosinophiles.........	3%	2 0%	5%	4%	
Lymphocytes........	29%	48 5%	25%	43%	
Monocytes..........	11%	13 5%	9%	3%	
Normoblasts.........	30/100 WBC	66/100 WBC	16/100 WBC	6/100 WBC	
Absolute number...	(11,715)	(12,600)			
Reticulocytes........	40%	34%			
Platelets............	210,000	165,000			

* Day prior to admission.
† Day following transfusion of 85 c.c. whole blood (citrated).
‡ Nucleated red blood cells not included.

control. Urine analysis: clear yellow; albumin, negative; sugar, negative; microscopic examination, negative; bile absent; urobilin positive 1:10. Stool was positive for bile pigments and urobilin, negative for frank and occult blood.

June 5, 1936: Gastric analysis: Free Hydrochloric Acid 10. Tuberculin, Schick, Wassermann tests negative.

COMMENT

The hematologic data in this case are sufficiently complete to permit a description of the anemia in terms of the physiology of the hematopoietic system. Thus the high bilirubin content of the blood with a positive indirect and negative direct Van den Bergh test indicates a hemolytic type of anemia. The presence of a high percentage of reticulocytes and of nucleated red cells indicates good regenerative powers and this was confirmed by the prompt response to a single transfusion.

Although congenital anemia has been recognized for many years, critical interest in the subject has been aroused, in America at least, by the paper of Diamond, Blackfan and Baty (1). They called attention to the close relationship between universal edema of the foetus, icterus gravis and congenital anemia.

Universal edema is characterized by its onset in utero, generalized anasarca, icterus, enlargement of the liver and spleen, anemia and erythroblastosis in the peripheral blood. Post mortem examination shows hematopoietic foci in the viscera far in excess of that found in the full term or premature newborn; these foci are rich in erythroblastic cells. The condition is frequently familial. Still birth is the usual occurrence. Icterus gravis is characterized by severe icterus, enlarged liver and spleen, severe anemia, sometimes slight edema, large numbers of erythroblasts in the peripheral blood, and foci of hematopoiesis and erythroblastosis in the viscera. Recovery may occur with prompt and repeated transfusion. This condition likewise is frequently familial.

Congenital anemia is the mildest of the three symptom complexes. Our case is typical of the group described by Diamond, Blackfan and Baty. The salient features referred to by them are anemia, erythroblastosis, liver and spleen palpable or enlarged, and jaundice. Some of the cases showed a familial incidence. None of their seven cases of congenital anemia came to autopsy but they emphasized the resemblance between the pathology of congenital anemia and the other two diseases by quoting the autopsy reports by Susstrunk and Schleussing of two cases of congenital anemia. These authors found "abnormal amounts of hematopoietic activity in the extramedullary tissue similar to that seen in erythroblastosis foetalis".

The close relationship of the three symptom complexes generally has been accepted. However, questions have arisen concerning the pathology and symptomatology of congenital anemia, its relation to erythroblastosis,

and, by implication, its etiology or, at least, pathogenesis. In the cases of Pasachoff and Wilson (3), of Brown and his associates (4), autopsy showed the absence of extramedullary hematopoiesis, hemosiderosis, and of erythroblastosis in the bone marrow, the essential pathological features ascribed to the symptom complex under discussion. In other words, these cases at post mortem indicated defective regeneration of erythrocytes, an absence of hemolysis, and of erythroblastosis.

Clinically also there is a group of cases of congenital anemia in which neither erythroblastosis, hemolysis nor the usual signs of active regeneration are found. Although several authors suggested that individual cases failed to show these characteristics (2, 3, 4, 5, 6), Cohen (7) pointed out with great clarity and emphasis these clinical and pathological distinctions and suggested that they fall into a separate group. His table is quoted in full:

	WITH ERYTHROBLASTOSIS	WITHOUT ERYTHROBLASTOSIS
Similar features:		
Erythroblasts	Present	Absent
Color index	High, above 1	High, above 1
Macrocytosis	Marked	Marked
Leucocytosis	High	High
Premature leucocytes	Present	Present
Placenta	Large	Large
Vernix caseosa	Often deep golden	Often deep golden
Amniotic fluid	Often deep golden	Often deep golden
Different features:		
Jaundice	Marked	Slight or absent
Bile in the urine	Present	Absent
Bile in the stool	Absent	Present
Urobilin production	Excessive	Normal
Bilirubin in serum	Very high	Normal
Edema	Sometimes present	Never present
Viscera	Erythropoiesis	No erythropoiesis
Hemosiderosis	Present	Absent

As a matter of fact, not all cases of congenital anemia can be placed in these two categories, since they differ in certain reactions—presence of leucocytosis, bilirubinuria, etc. In general it seems wrong to look upon these symptom complexes as fixed conditions; rather they are "moving pictures" representing an interplay of conflicting and compensatory forces. Cohen has done a distinct service in indicating that there are variations in the essential symptomatology and pathology—the symptoms and lesions involved in erythroblastosis, hematopoiesis and hemolysis. Pasachoff and Wilson consider the essential lesion in their case of congenital anemia without erythroblastosis to be a "defect in the erythrocytogenic system"; and Stransky (5) applied a similar and briefer term to two similar cases of his own, "aregenerative anemia".

In looking through the literature one is tempted to classify cases of congenital anemia as with or without erythroblastosis, hemolytic or non-hemolytic and regenerative or aregenerative. Indeed, but for incompleteness of data bearing on hemolysis and regeneration, this could be done. Diamond and his associates refer to a "terminology more descriptive of this pathologic state and in accord with common usage . . . : universal edema of the fetus with erythroblastosis, icterus gravis neonatorum with erythroblastosis and anemia of the newborn with erythroblastosis." Obviously this terminology cannot be applied to all cases of congenital anemia. The facts suggest that any qualifying term added to anemia of the newborn should be descriptive of the condition in the particular case. Thus the case we are reporting would be called congenital anemia with hemolysis, regeneration, and erythroblastosis.

These clinical and pathological differences in different cases need not modify the conception of a single etiology of universal edema, icterus gravis and congenital anemia. For it is biologically sound to believe that a single factor effective possibly at different stages in the development of the newborn, working with different degrees of intensity upon organisms that react differently, may cause such diverse conditions as universal edema, icterus gravis and the various types of congenital anemia.

The safest treatment is transfusion. Some cases have recovered spontaneously (8), and others with liver therapy (9). However, the rapid drop in hemoglobin and, at times, the sudden collapse with death (3, 4) indicate the risk in postponing transfusion.

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MASSIVE INFARCTION OF THE LIVER

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[From the Medical Service of Dr. B. S. Oppenheimer]

True anemic infarction of the liver is a comparatively rare occurrence. Massive infarction on the basis of embolization has been reported only twice. For these reasons, and because of a possible correlation between the clinical and pathological findings, the following case should prove of interest.

CASE REPORT

History (Adm. 397775). The patient, a 34 year old housewife, sought admission because of sharp pain in both legs for five days. Nine years before, she had been told that she had a cardiac murmur. For six years she remained asymptomatic; then increasing dyspnea on exertion, orthopnea, and pedal edema developed and for one year she had to take maintenance doses of digitalis. Five days before admission, she suddenly experienced severe colicky pain in the right costovertebral region, the pain radiating anteriorly and into the right groin. Sharp pains in both legs followed immediately and lasted for fifteen minutes. During the next two days there were two similar episodes of pain in the legs and the feet and legs became cold and numb.

Examination. The patient was an obese young woman, moderately cyanotic and slightly orthopneic. Slight venous pulsations were present in the neck. The lungs were clear. The heart was markedly enlarged to the left and right. A rumbling diastolic murmur was heard over the apex, with diastolic shock and a split second sound in the pulmonic area. The rhythm was totally irregular; the apical rate was 108, the radial rate 96; the pulse deficit was therefore 12 beats per minute. The systolic blood pressure was 110 mm. of mercury, the diastolic, 80. The liver edge could not be felt but liver dulness extended one finger's breadth below the costal margin. The spleen could not be palpated. Both lower extremities were cold below the knees. No pulsations could be felt in the popliteal, posterior tibial or dorsalis pedis arteries.

The total leucocyte count was 15,000 per cu. mm., with 64 per cent polymorphonuclear leucocytes, 28 per cent lymphocytes, 6 per cent monocytes, and 2 per cent eosinophiles. The urine was negative except for the presence of occasional red cells. The erythrocyte sedimentation time was 38 minutes for 18 mm. The blood Wassermann test was negative; blood urea nitrogen was 16 mgm. per 100 c.c., and blood sugar was 90 mgm. per 100 c.c. Oscillometry gave readings of 0.25 of a scale division below the right knee and zero below the left knee. An electrocardiogram revealed

auricular fibrillation, the QRS complex was slurred and of moderately low voltage, with T-waves of low amplitude.

Course. For a period of one week the patient ran a low-grade febrile course and the legs seemed to be improving gradually. The ventricular rate of the heart was slowed and the pulse deficit abolished by digitalis. Two days after admission she complained of increasing abdominal pain. At first, slight generalized abdominal tenderness was noted; this was somewhat more marked over the right side of the abdomen. Examination of stool, urine and a blood count showed no significant change after this. After twenty-four hours the abdominal signs became localized in the right upper quadrant where tenderness and spasticity of the abdominal wall could be elicited. Right costovertebral angle tenderness was also present. Abdominal puncture in the left lower quadrant twelve hours later yielded several drops of turbid fluid containing many polymorphonuclear leucocytes but no organisms. Marked rebound tenderness persisted in the right upper quadrant. Another episode of severe pain in the right leg occurred and the leg gradually became mottled and cold. Six days after the onset of abdominal pain, the patient's temperature rose rapidly and two days later just before death reached 108°F.

Diagnosis. The question of the etiology of the abdominal condition aroused much discussion. With the evidence of previous embolization to the renal artery and to the arteries of the lower extremities, the first assumption was that intra-abdominal embolization had occurred. However, the suspicion of mesenteric thrombosis could not be confirmed because of the absence of gross and occult blood in the stool. A fresh renal infarction was unlikely without some degree of hematuria. The early generalized abdominal pain localizing in the right side of the abdomen, although mainly in the right upper quadrant, suggested a coincidental appendicitis and the surgical consultants urged an exploratory laparotomy. In view of the evidence of continued embolization, it was felt, however, that the abdominal condition was probably on the basis of the latter, and that, in any case, the risk of surgical intervention was too great considering the patient's general condition.

NECROPSY FINDINGS

The *heart* weighed 390 grams. The right ventricle was moderately dilated and hypertrophied, the left auricle markedly dilated. Two thrombi were loose in the left auricle, their cut section showing a dark red, soft, moist core. Posteriorly, there was an area about 2.5 cm. in diameter in which the endocardium was thickened, granular, and grayish-yellow. Marked stenosis of the mitral orifice was found with thickening and fusion of the valves. The left ventricle was moderately hypertrophied. There was moderate stenosis of the aortic orifice. Microscopically there were small, scattered, stellate areas of myocardial fibrosis; some of these were

perivascular. There were scattered interstitial collections of polymorpho-
nuclear leucocytes, lymphocytes and plasma cells.

The *aorta* showed a firm, cylindrical blood clot lying loose just proximal
to the bifurcation. The left internal iliac artery contained a dark red blood
clot firmly adherent to the wall. The arteries of the legs could not be ex-
amined.

The *lungs* showed no significant changes.

The *liver* weighed 1320 grams. The capsule was thin and smooth. The
right lobe was moderately firm and the surface a mottled brownish-red.
The left lobe, with the exception of an area extending 2 cm. to the left of
the falciform ligament which was similar to the right lobe, was soft and
flabby. The surface here was a mosaic of irregular mottled areas. On
section the right lobe and the right extremity of the left lobe were greenish-
yellow in color. Bile oozed from the cut surface. The architecture of the
liver could be made out only with difficulty. The central areas, when
visible at all, appeared as reddish-brown pin-points. The remainder of
the left lobe was dark green and the architecture could not be made out at
all. There was a sharp line of demarcation between the soft, homogeneous,
dark green left lobe and the remainder of the liver, the line of demarcation
being 2 cm. to the left of the falciform ligament. The *left hepatic artery*
just distal to its origin from the hepatic artery proper was occluded by a
dark red firmly adherent blood clot approximately 1.5 cm. long. The
portal and hepatic veins showed no changes.

On microscopic examination the infarcted left lobe showed islands of
tissue with coagulation necrosis of the liver cells, the latter appearing as
homogeneous, deeply eosinophilic fragments. Some of these cells showed
small, pyknotic nuclei. The outlines of the sinusoids were distinct.
There was marked infiltration of the surrounding areas with polymor-
phonuclear leucocytes, macrophages, lymphocytes and red cells. The
remainder of the liver showed central necrosis and atrophy.

The *gall-bladder* showed thickening of the serosa. The mucosa was
thick and slightly roughened and partially desquamated in some areas.
The common bile duct near its upper end contained a black mulberry
stone about 1.2 cm. in diameter, which could be cut without difficulty.
The cystic and hepatic ducts were moderately dilated. The cystic artery
was not examined. Microscopically the gall-bladder showed severe
diffuse inflammation. All the layers of its wall were markedly congested
and edematous and infiltrated with plasma cells, lymphocytes, and a few
polymorphonuclear leucocytes.

The *right kidney* showed one large and several smaller infarcts.

DISCUSSION

Aside from the rarity of massive infarction of the liver, the case is of
interest since it raises the question of possible correlation between the
clinical picture and the unusual pathological findings. Clinically the

attention was drawn to the right upper quadrant of the abdomen. In this region there was marked tenderness, rebound tenderness, and slight to moderate spasticity of the abdominal wall. A smaller amount of tenderness was also present over the right lower quadrant and right costovertebral angle. There was no vomiting; the leucocyte count remained unchanged; stools and urine were negative; and the temperature curve was not significantly altered until six days after the onset of abdominal pain, rising to 108°F. only shortly before exitus. That there was some generalized peritoneal reaction was demonstrated by the discovery by abdominal puncture of a few drops of turbid fluid containing many polymorphonuclear leucocytes.

If such a clinical picture in a patient with evidence of infarction elsewhere could be definitely ascribed to hepatic infarction, the clinical diagnosis of the condition would be established and surgical intervention would not be considered at all. The disturbing element in this case was the finding at post mortem examination of a concomitant cholecystitis and choledocholithiasis. That these were at least partially responsible for the clinical picture cannot be denied. In future cases of hepatic infarction, a careful analysis of the symptomatology should be made in order to determine whether hepatic infarction alone can give rise to the constellation of signs and symptoms presented by this case.

It has been amply demonstrated (1 et al.) that true anemic infarction of the liver occurs only when the hepatic arterial supply has been obstructed. The development of infarcts following the arterial obstruction is dependent upon the presence or absence of collateral circulation. In the present case, the obstruction was caused by the lodgment of an embolus in the left hepatic artery just distal to its origin from the main hepatic artery. This case also illustrates the fact that the arterial supply of the left lobe of the liver does not extend to the falciform ligament.

Pass (2) reviewed the literature on hepatic infarction. Omitting infarctions resulting from trauma or ligation of the hepatic arteries, he was able to collect from the literature only fifty-two cases of true anemic infarction. Of these, twenty-one were the result of embolization, the majority occurring in subacute or acute bacterial endocarditis; only four originated in mural thrombi. Where other than embolic factors were responsible for the infarction, periarteritis nodosa was the most common underlying disease, followed by thrombosis, endarteritis and hypoplasia of the hepatic artery. Pass adds two cases of his own, one caused by compression of the hepatic artery by extensive carcinomatous metastases and the other occurring in a case of periarteritis nodosa. Omitted from the review are five cases reported by Lund, Stewart and Lieber (3). Of these, three occurred in cases of bacterial endocarditis, a fourth in which the etiology was not clear, and lastly a fairly large infarct originating in a mural thrombus at the site of a coronary artery infarction.

Only two cases of massive infarction of the liver have been reported.

Chiari's case (4) is the most spectacular, one in which the entire liver showed the picture of parenchymal necrosis following obstruction of the main hepatic artery just proximal to its division by a large embolus. The origin of the embolus was cardiac but the possibility of a bacterial endocarditis was not definitely ruled out in the paper. The case presented by Cioni (5) was that of almost complete infarction of the right lobe of the liver by an embolus from an auricular thrombus.

If one omits those cases resulting from trauma or ligation of an artery, and excludes the so-called Zahn's infarcts, the infarct-like red atrophy secondary to occlusion of branches of the portal vein, a total of fifty-seven cases of hepatic infarction have been reported. Nevertheless, it is probable that a review of the autopsy material in any large hospital would disclose additional cases. In The Mount Sinai Hospital during the past ten years, five cases of true anemic infarction of the liver have been found, in addition to the one reported at length in the present communication. These cases may be briefly outlined as follows:

Case 1. Adm. 347908. Male, 56 years of age. Carcinoma of stomach with metastases to regional lymph nodes and liver and thrombosis of the hepatic arteries. Multiple small infarcts of the liver present.

Case 2. Adm. 299079. Female, 18 years of age. Acute bacterial endocarditis due to staphylococcus aureus. Numerous pin-point and pea-sized abscesses present in the liver with few wedge-shaped infarcts; many vessels almost choked with gram-positive cocci.

Case 3. Adm. 309486. Male, 42 years of age. Subacute bacterial endocarditis. Small infarct (1.5 cm. in diameter) in the right lobe of the liver.

Case 4. Adm. 367887. Male 20 years of age. Periarteritis nodosa. Several infarcts 2-3 cm. in diameter.

Case 5. Adm. 349909. Male, 42 years of age. Rheumatic heart disease with auricular fibrillation; auricular thrombus. Small infarct (2 cm. in diameter) in the right lobe of the liver.

The various etiological factors in even such a short series as this parallel in general the distribution of causes in the fifty-seven cases reported in the literature.

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RETINOPATHY AND DEGENERATIVE NEURONOPATHY IN DIABETES

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In recent years numerous reports have been published of specific retinal lesions occurring in the diabetic. Controversy has been active concerning the relationship of the diabetic process to the etiology of the retinal lesions. There is still a sharp difference of opinion on this subject, one group of observers maintaining that retinal lesions occurring in the diabetic are a result of causes other than the diabetes, i.e. arteriosclerosis, hypertension or nephritis; and another group that the lesions are secondary to the diabetes alone. More recently some attention has been directed again to the clinical, pathological, and chemical aspects of neuronopathy in the diabetic. The following case is of interest since it presents in a young diabetic both retinal and neurological changes.

CASE REPORT

History (S. O., Adm. 386862). A 36 year old clothing salesman was admitted to the hospital complaining of dimness of vision of three months' duration. His mother had died, at the age of 66 years, of diabetes. His past history was negative except for transient episodes of fever, malaise, coryza, and cough occurring one to two times yearly for the past twenty years. He was a known diabetic of fifteen years' duration, the disease having been first discovered during a routine examination for life insurance. It had not been sufficiently severe to require insulin, nor to have caused loss of weight which had kept a steady level at about 115 pounds. He had been hospitalized once twelve years ago elsewhere for a short period in order to regulate the diabetes. Since that time some dietary precautions had been observed. During the past two years he had been taking 15 units of insulin before the evening meal. Urine tested before retiring on an occasional evening during the month had at times revealed traces of sugar. He noticed impairment of vision two years before the present admission when his right eye became reddened for a few days. There had been a gradually progressive dimness of vision in that eye until three and a half months before admission when he arose one morning with a painful, blood-shot left eye. The pain had not been severe and the symptoms continued for three days when he first noted diminishing vision in the left eye. He consulted an ophthalmologist who told him he had "hemorrhages" in his left eye. The "conjunctival" reddening cleared in one week but the visual impair-

ment persisted and progressed steadily to the time of admission, when he
was able to read only with the aid of a magnifying lens.

Examination. The patient was a well developed and well nourished
white male. His heart, lungs, and abdomen showed no abnormal findings.
The pulses were equal, regular, synchronous and of good quality. There
was marked thickening of all peripheral vessels. No pulsations were felt
in the left dorsalis pedis. The extremities showed no change in color or
temperature. The blood pressure was 120 systolic and 80 diastolic. The
skin of the pretibial regions showed a generalized light brown pigmenta-
tion and a glossy atrophy. The palms were of an orange-yellow color.
The pupils were irregular, the left oval, both reacting sluggishly to light
and somewhat better in accommodation. The conjunctivae and sclerae
were normal; there was no exophthalmos. The fundi disclosed discs of
normal color, edges a trifle hazy especially in the left fundus where some
powdery exudate covered the upper margin. In both eyes the macular
and perimacular regions were studded with discrete and confluent masses of
orange-yellow deep exudates, recent and old. Both fundi were speckled
with hemorrhages. Most of these were recent and in the deeper retinal
layers. A large number of pin-point hemorrhagic spots were scattered
throughout. The veins were overfilled, the arteries narrowed, often in-
denting the veins. Visual function tests disclosed markedly diminished
visual acuity, to less than 20/200 in each eye. The patient was unable to
see central spots of perimeter, campimeter, or tangent screen. The super-
ficial reflexes were equal but depressed. The knee jerks and ankle jerks
were absent on both sides. The biceps jerks were absent and the triceps
jerks sluggish. There were no pathological reflexes. Power in the ex-
tremities and sensation, including vibratory and position sense, were
intact. Oscillometric readings of the lower extremities disclosed a slight
diminution of arterial pulsation, but roentgenograms failed to reveal cal-
cifications in the vessels.

Laboratory Data. The Wassermann and Kahn reactions of the blood,
and the Wassermann reaction of the spinal fluid, were negative. Colloidal
gold reaction of the spinal fluid was also negative. The hemoglobin was
90 per cent; the white blood cell count was 5,000 with a normal differential
count; the blood urea, 14 mgm. per cent; fasting sugar, 325 mgm. per cent;
cholesterol, 355 mgm. per cent.

Electrocardiographic examination revealed sinus tachycardia with low
T-1 and diphasic T-4, which changes were interpreted as possible evidence
of involvement of the ventricular muscle.

Course. The patient's diet was gradually increased to one of Carbo-
hydrate, 300 gm.; Protein, 100 gm.; and Fat, 40 gm.; with Insulin 20–15–15
units before each meal. On this regime while in the hospital he continued
to spill a small amount of sugar. He was discharged after several weeks
of observation. There had been no improvement in either the visual or
neurological status.

On reexamination eight months later the patient stated that he had followed his diet carefully and had consistently used insulin, having gained fourteen pounds in weight since discharge. Urine specimens examined several times daily had never contained sugar. There were occasonal fleeting insulin reactions. The pupillary and deep reflexes had remained unchanged, though there were no neurological symptoms. The fundi showed changes almost identical with those seen on the first admission. During the past three weeks he had been seeing shadows with the left eye moving in the same direction as movements of the eyeball. The left fundus showed several deep, large hemorrhages not seen previously.

COMMENT

Although diabetes had been discovered in this patient as far back as fifteen years before his admission to the hospital, the disease process had apparently not been severe. The mild degree of the diabetes was indicated by the absence of notable glycosuria and by the preservation of a good state of nutrition, without episodes of ketosis despite the frequent incidence of upper respiratory infection. The retinal changes in this patient corresponded in almost every detail with the "central punctate retinitis" described by Hirschberg (1) in 1890, the second type of Wagener, Dry, and Wilder (3). The absence of any of the findings of impaired renal function with normal blood urea, the absence of hypertension or evidence of preexistent hypertension, and the absence of any sclerotic changes of the retinal vessels indicated the relationship of the retinal changes in this case to the diabetic process. It is true that there were slight T-wave abnormalities in the electrocardiogram suggestive of involvement of the ventricular muscle, and slight impairment of the oscillometric readings. Both of these indicated a possible mild arterial occlusive process, but the absence of arteriosclerotic changes of retinal vessels as determined by direct examination militated against the consideration of the retinal changes as an expression of a vascular disease and necessitated the implication of the diabetes alone.

The neurological changes of depressed deep reflexes and sluggish pupillary reactions are a frequently found combination of neuronopathy in the diabetic. Although few reports appear in the literature concerning the coincidental finding of neuronopathy and retinitis in the diabetic, this association is probably not uncommon, in view of the fact that retinal lesions have been found in as high as in 38 per cent of a series of diabetics (Soskin, (5)) and neurological disturbances in more than 50 per cent (Jordan, Randall, Bloor (7)). In Wagener's series, 25 per cent of the patients with retinal lesions also presented evidences of neurological disturbances, while in the control series of diabetics, without retinal lesions, only 8 per cent presented such disturbances.

Despite adequate control of the diabetes, there had been no improvement in the neurological status of the patient, while the retinal changes had

definitely progressed. The prognosis in this case is extremely poor, with the probability that hemorrhage in the vitreous and "retinitis proliferans" may develop sooner or later.

<div align="center">DISCUSSION</div>

Several recent reviews have contributed definite statistical evidence in support of the belief that specific retinal lesions occur in the diabetic and that these lesions can be ascribed to the diabetes as the sole etiologic agent. Following Hirschberg's (1) classification and description of retinal changes in 1890, several papers appeared with descriptions of cases of so-called "central punctate retinitis." Among the earliest statistical studies was that of Friedenwald (2) who found 33 cases of central punctate retinitis in his series of diabetics. In an equal number of non-diabetics, he found only 18 cases of central punctate retinitis. He therefore concluded that the diabetes must contribute to the development of this lesion.

In a review of over 1,000 cases of diabetes Wagener, Dry, and Wilder (3) found several distinct types of retinal lesions, all being phases of a single underlying process, and all being characteristic of the disease. The total incidence of retinal lesions in this series was 17.7 per cent, with 23 of the cases (12 per cent of all the diabetic patients with hemorrhagic retinal lesions) showing a blood pressure of less than 140 systolic and 90 diastolic. There was no clear evidence of disease of the arteries or kidneys, there was no arteriosclerosis of the retinal vessels, and seven of this group were below 40 years of age. There was no correlation in this series between the severity of the disease and the severity of the retinal lesions, but there was definite progression of the lesions with increased duration of the disease. In this regard it is interesting to note that in 1921 the incidence of retinopathy among diabetics was 12.3 per cent, while in 1934 it had risen to 17.7 per cent. This increase is probably due to the increased duration of the disease, with more young diabetics now passing into the older age groups in which such lesions are found. Struble (4) has recorded a case of a 39 year old woman who was observed in his clinic for a hemorrhagic fundus lesion. She was known to have had diabetes for four years. She was kept sugar free without insulin on dietary restriction but, despite this apparent adequacy of treatment, developed a retinitis proliferans in the course of fourteen months. It was subsequently discovered that this patient ran a persistently elevated blood sugar without glycosuria and required 30 units of insulin daily to maintain a normal level of blood sugar. This case is an excellent example of the increasing severity of the retinal lesion with increased duration of the diabetes. Time will show whether protamine insulinate, so effective in restoring normal metabolic activity in diabetics, is equally useful in reducing the incidence of diabetic retinopathy.

The retinal lesions described by Wagener consist, in the earliest stage, of tiny punctate hemorrhages occurring in the vicinity of dilated venules in the macular region. They at first are round and situated in the deeper

retinal layers; later they may become larger and more widespread. Later in the course of the retinopathy the picture of "central punctate retinitis" develops. It consists of the hemorrhagic lesion upon which are superimposed a few shiny, irregular punctate exudates. The latter are usually situated deep near the fovea, but in time may appear in any part of the retina, ultimately fusing into large necrotic-looking plaques which interfere with central vision. In each of these phases of retinal change the arteries show no lesions although the veins are frequently somewhat dilated. Similar lesions have been noted in the diabetic fundus in the presence of hypertension, without changing the character of the lesion, which is pathognomonic of diabetes. Occasionally, in the presence of hypertension and angiospasm there appear larger, more edematous exudates. They are scattered throughout the retina and are superimposed on the typical lesions of the central punctate retinitis. Finally, as a last stage in the development of diabetic retinopathy, marked venous lesions, resembling those seen in tuberculosis, may develop. Here the veins become dilated, cyanotic, and present numerous nodular dilatations with intervening constrictions suggesting mural thrombi. These are usually associated with large hemorrhages, with an occasional hemorrhage into the vitreus, giving rise to vitreus proliferation of scar tissue, the so-called "retinitis proliferans." In such instances contraction of the scar may result in retinal detachment.

Soskin and Falk (5) observed and recorded the fundus changes in 150 diabetics and 150 non-diabetics of approximately the same age group. They found retinopathy in 33 per cent of the patients in the diabetic group and in only 6 per cent in those of the non-diabetic. The criteria used by these observers for the diagnosis of central punctate retinitis were essentially the same as those described by Wagener. There were no cardiovascular complications in 60 per cent of their cases of central punctate retinitis (9 of 15) and in 8 of these cases the blood pressure was low. They were able to find no correlation between the occurrence and the severity of the retinal lesions on the one hand and either the duration or severity of the diabetes on the other. Where there was good cooperation in treatment in 2 cases, the lesions disappeared gradually with complete restoration of the fundus to its normal state. Wagener also found 4 cases in whom complete resolution took place. This, of course, is the exception in diabetic retinopathy.

While it would seem that the retinal lesions of a specific character which develop in the diabetic are due to diabetes alone, very little has been offered to account for the manner in which the diabetic process affects the retina to produce these characteristic changes. Hyperglycemia, hypercholesteremia, and ketosis immediately suggest themselves as possible causative factors and have been respectively offered in explanation, since they are conditions also common to diabetes. These explanations, however, provide only biochemical terms, without describing the manner of

operation of these altered biochemical states upon the structures in-
volved.   Therefore we must await more accurate knowledge of patholog-
ical and chemical factors operative in retinal lesions.

Bouchard (6) in 1881 first observed that knee jerks are often absent in
the diabetic.   Since then Jordan, Randall and Bloor (7) found that about
50 per cent of diabetics show evidences of organic disease of the nervous
system.   Thus it was noted that, in 461 diabetics, 45.3 per cent showed
depressed or absent patellar and Achilles reflexes.   Lesions have been found
in the brain, spinal cord, dorsal roots and spinal nerves.   The central
lesions were found insufficient to account for the diabetic neuronopathy,
since disease changes in nerves were frequently found in peripheral por-
tions, while the central parts remained uninvolved.   Similarly, the view
became prevalent that disease alterations in the nervous system were due
to the metabolic disturbance associated with diabetes.   In confirmation of
this concept it was noted that absent knee jerks in the diabetic occasionally
return, that signs increase with increasing cachexia, that improvement
occurs with improved nourishment, and that neurologic manifestations are
more common in the mild, old diabetic than in the young and severe dia-
betic.   However, since the young, severe diabetics very seldom develop
neurologic disturbances, it cannot be the altered metabolism alone which
produces the change in the nervous system.   It is more likely that some
other factor, which results from the metabolic disturbance acting over a
long period of time, is responsible for the condition.

Chemical studies were made by Jordan, Randall, and Bloor (7, 8) on
diabetic nerves obtained at autopsy or by amputation in 20 cases.   These
nerves were all obtained from old patients with deficient circulation, in
whom the disease had been of an average of eight years' duration, fairly
well controlled, with no history of syphilis, alcoholism or other focus of
infection.   A similar number of nerves were used from a control group of
approximately the same age.   There were found significant chemical
changes in the diabetic nerves.

1. Phospholipid, cholesterol and cerebroside values of diabetic nerves
were found considerably below the averages found in the normal nerves used
for control.

2. The greater the vascular disease, and the more peripheral the segment
of the nerve examined, the more marked were the chemical changes.

3. The effect of severity, duration and control of the diabetes was slight
or negatived by other factors.

4. Lipoid abnormality appeared in the absence of clinical neuronopathy,
but the degree of abnormality increased as the clinical signs progressed.

The investigations demonstrated also that the nerve degenerations of the
diabetic increase in direct ratio to an increasing vascular damage.   In the
non-diabetic, however, there is not the same proportionate increase in
nerve degeneration, with the increasing vascular damage.   From this Jor-
dan concluded that vascular disease is not the sole cause of degenerative

nerve changes in the diabetic and that these changes may be due to the same defective fat metabolism which may be the contributing cause of the vascular disease. This is especially likely in view of the fact that the diabetic nerve changes are found chiefly in the fat-containing myelin sheath.

The clinical manifestations of diabetic neuronopathy may be as varied as those of true tabes. Pains, cramps, paresthesias, and other forms of sensory disturbance, bladder disturbances, hyporeflexia, gastric crises and pupillary findings, indistinguishable from those of true tabes, may be found in varying combinations. The tabes of diabetes, however, has not been known to cause the great ataxia and final incapacity of all locomotion which has been seen in the far advanced syphilitic tabetic.

The prognosis in instances of neural involvement in the diabetic is determined by the mode of onset of neuronopathy. Accompanying an acute hyperglycemia, the prognosis is good. The neurologic signs disappear as the diabetes is brought under control. Where there is a concomitant marked vascular change, characterized by mild symptoms beginning insidiously and progressing slowly over a period of years the prognosis is usually poor.

CONCLUSION

1. A case of diabetes in a young male with severe retinal changes and mild neurological changes not associated with renal, hypertensive, or significant vascular disease is presented.

2. A brief review of some of the recent descriptions of retinal and neurological changes in the diabetic is presented.

3. Some evidence is presented to support the view that a specific retinopathy occurs in the diabetic, and that the neuronopathy of diabetes is related to the effects of the metabolic disturbance.

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SCHWANNOMA OF THE CAUDA EQUINA

Five-Year Result after Roentgen Therapy

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It is common knowledge today that many spinal cord tumors yield successfully to surgical removal. This is especially true of the extramedullary growths, including meningioma, fibroblastoma, lipoma and hemangioendothelioma. However, sarcoma, angioma, lymphosarcoma and some neuroglioma (Schwannoma) are varieties of neoplasms which are not surgically remediable or only incompletely so. Radiation therapy is therefore frequently called upon in the treatment of these latter conditions (Flatau, (1), Bailey and Bucy (2), Paumelle (3)).

Schwannoma (neuroglioma) is a new growth which is usually considered to be unresponsive to the effect of the roentgen rays. (Sicard et al (4).) The case to be reported in this article deals with a Schwannoma of the cauda equina which responded very favorably to radiation therapy.

Penfield (5) says that these tumors are usually vascular, usually have areas of degeneration and are always attached to the nerve roots. They are always benign in that they do not metastasize. They may recur locally unless removal is complete. Usually, it is impossible to secure complete removal of the tumor and yet preserve the integrity of the nerve function. As to the origin of this form of tumor, Masson (6) states that they arise from the cells of the sheath of Schwann and have no nerve fibers. A widely accepted theory promulgated by Harrison (7) states that the cells of the neurilemma sheath of Schwann migrate outward from the neural crest and are probably ectodermal derivatives (Figure 1).

CASE REPORT

History (W. M. Adm. 331589). A white male, age 45 years, was admitted on October 26, 1931, to the Neurological Service of Dr. I. Strauss because of pain in the lower back. The pain was first present three and one-half years before admission and the patient had never been really free from it since the onset. The pain began in the region of the lower back and radiated down the left buttock along the posterior aspect of the left thigh and leg to the sole of the foot. There was also radiation of the pain down the right buttock and for a short distance down the posterior aspect of the right thigh. At times, the pain would be very acute and would keep him awake at night. The patient had had diathermy and a course

of baths at a Mineral Springs sanitarium—all without relief of symptoms. Six months after the onset, an exacerbation of pain was accompanied by edema of both legs. Jaundice occurred five weeks before admission; it was learned that the patient had taken large doses of "Atophan" over a period of four weeks. A decrease in libido was noted but there were no sphincter disturbances.

The past history was negative except for mastoidectomy twenty-five years previously.

Examination.—There was moderate icterus, enlargement of the liver, edema of both legs, and tenderness over the sacrum. The left ankle jerk was absent. A mild hypalgesia on the left side, involving the second to fifth sacral dermatomes, and slight perianal hypalgesia on the right were present.

Course: Although the patient was considered at first to be suffering from lumbosacral radiculitis, the consensus of opinion later swung to the suspicion of cauda equina tumor (Dr. Strauss had suggested this possibility when he referred the patient to the hospital). With regard to the icterus,
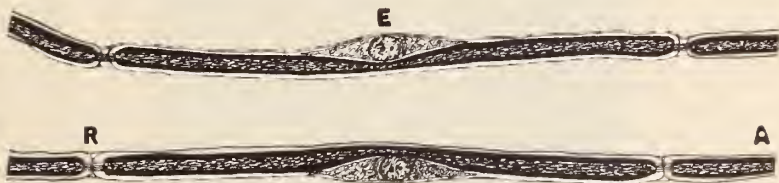
FIG. 1. Diagram after Schäfer and Spielmeyer
R—Node of Ranvier; A—Neurilemma; E—Nucleus

it was the opinion of Dr. Baehr that the patient had a cirrhosis of the liver which had made him more sensitive to the "Atophan". The blood chemistry included an icteric index of 30, a Van den Bergh reaction which was delicately positive on the direct and with the indirect was 1:300,000.

Roentgen examination of the spine showed a widening of the canal of the fifth lumbar vertebra, with destruction of the lamina on the left side of the fourth lumbar vertebra. The first spinal puncture between the third and fourth lumbar vertebrae yielded xanthochromic fluid but no block. Another puncture was performed between the fourth and fifth lumbar vertebrae showing evidence of a partial block and xanthochromic fluid which coagulated spontaneously. The spinal fluid showed an increase of the total protein, i. e. 98 mgm. per cent.

Operation: On November 10, 1931, exploratory laminectomy was performed under spinal anesthesia by Dr. Ira Cohen. His observations were as follows:—"At lower border of fourth lumbar vertebra, the vertebral canal was widened and dura thinned out by a vascular tumor which had all but perforated the dura. On opening the dura, this very vascular tumor was seen to lie among the roots of the cauda equina and extend

down into the sacrum and upward beyond the third lumbar vertebra. Clinical diagnosis:—Sarcoma.   Biopsy taken but tumor was not removed."

Histological report (Dr. Globus): "Gliogenous tumor arising from peripheral nerve (Schwannoma with spongioblastic features)" (Figure 2).

November 20 to December 19, 1931—Radiation therapy based on the method of Coutard (8) was given as follows:

Lumbar spine (1–5) direct........................	3380 r
Lumbar spine (right).............................	900 r
Lumbar spine (left)......................	800 r
Total..	5080 r (with back scattering).

A radiodermatitis with moist desquamation occurred ten days after the last treatment.   This reaction healed completely in one week.
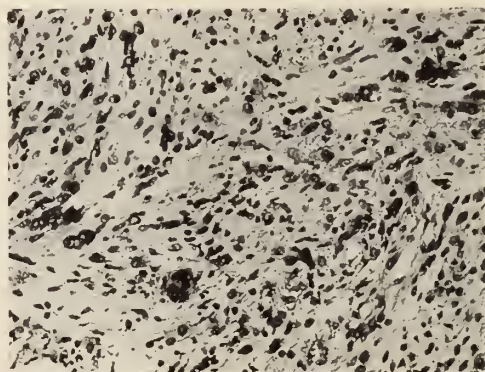
Fig. 2. Schwannoma with spongioblastic features

Physical Factors Employed

K. V.	M. A.	FILTER	HALF VALUE LAYER	DISTANCE	SIZE OF PORTAL	DAILY DOSE
180 (constant, potential)	4	2 mm. Cu +1 mm. Al	1.4 mm. Cu	50 cm.	8 x 15 and 12 x 15 cm.	175–200 r (tissue dose)

Postoperative Course.   Following the operation and radiation therapy, the patient felt only an occasional twinge of pain over the left buttock. The objective findings remained about the same, viz., absent left ankle jerk and hypalgesia in S 3–4–5 on the left.   For a period of time, there was some frequency of urination which gradually disappeared.   Integrity of the sexual vigor was restored and about a year ago the patient's wife gave birth to a female infant.   At the time of the present writing, the objective findings are similar to those noted above and the patient states

that occasionally he is aware of a fleeting pain in the left buttock with some corresponding numbness. He is working steadily without experiencing any disability whatsoever. The irradiated skin presents no evidence of any injury except for absence of hair in that region. The skin is smooth, soft, and shows only a very mild pigmentation.

SUMMARY AND REMARKS

A case of inoperable tumor of the cauda equina (Schwannoma) is reported in which recovery has taken place after exploratory laminectomy and extensive roentgen ray therapy. The patient has been comparatively free of symptoms for the past five years.

The favorable result obtained in this patient is assumed to be due to two factors: (*a*) the large total amount of radiation administered within a limited period of time, and (*b*) the histologic character of the tumor which seemed to lend itself to beneficial response to radiation, i. e. its gliogenous and vascular features.

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AN ELECTROCARDIOGRAM CHARACTERISTIC OF CORONARY THROMBOSIS IN A PATIENT WITH AORTIC STENOSIS

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The occurrence of angina pectoris in calcareous aortic stenosis is not uncommon and has recently been discussed by Boas. Several of his cases with heart failure simulated coronary thrombosis clinically. The following case is reported particularly because, while the electrocardiographic changes, in addition to the clinical course, were characteristic of coronary artery thrombosis, yet no evidence of coronary artery involvement was found at necropsy. The electrocardiographic abnormalities have not been observed previously and are important because they shed light on the mechanism of production of the electrocardiogram considered pathognomonic for coronary thrombosis.

History (P.K., Adm. 390639). A 65 year old housewife gave a history of dyspnea on exertion and orthopnea for five years. She experienced two attacks of severe precordial pain associated with dyspnea respectively six and two months prior to admission. In each instance the pain disappeared after several days. Five days after the second attack the patient began to cough and raise bloody sputum. There was pain in the right chest posteriorly and a rise of temperature.

Examination. The patient was acutely ill, dyspneic, orthopneic, and cyanotic. Dulness and diminution of breath sounds and voice over the lower right chest anteriorly and posteriorly were observed. The heart was moderately enlarged to the left. Over the aortic area was a rough systolic thrill and a loud systolic murmur. The peripheral vessels were sclerosed. The blood pressure was 120 systolic and 70 diastolic. The liver edge was palpable 2 cm. below the costal margin. There was no edema.

A diagnosis was made of coronary thrombosis in a woman with coronary sclerosis and sclerotic stenosis of the aortic valve, cardiac failure and pulmonary infarction. The electrocardiogram appeared to corroborate the diagnosis, for the R-T transition was strikingly elevated in leads III and IV and depressed in lead I. This was considered characteristic of coronary artery occlusion. In addition auricular flutter and complete auriculoventricular dissociation was present, with occasional premature beats. There was left ventricular preponderance and high voltage of the QRS

complex, indicating a large left ventricle.   The patient was placed in an oxygen tent but without relief and she died suddenly on the second day.

Post mortem examination revealed rheumatic heart disease with mitral stenosis and insufficiency and fish-mouth aortic stenosis, both valves being
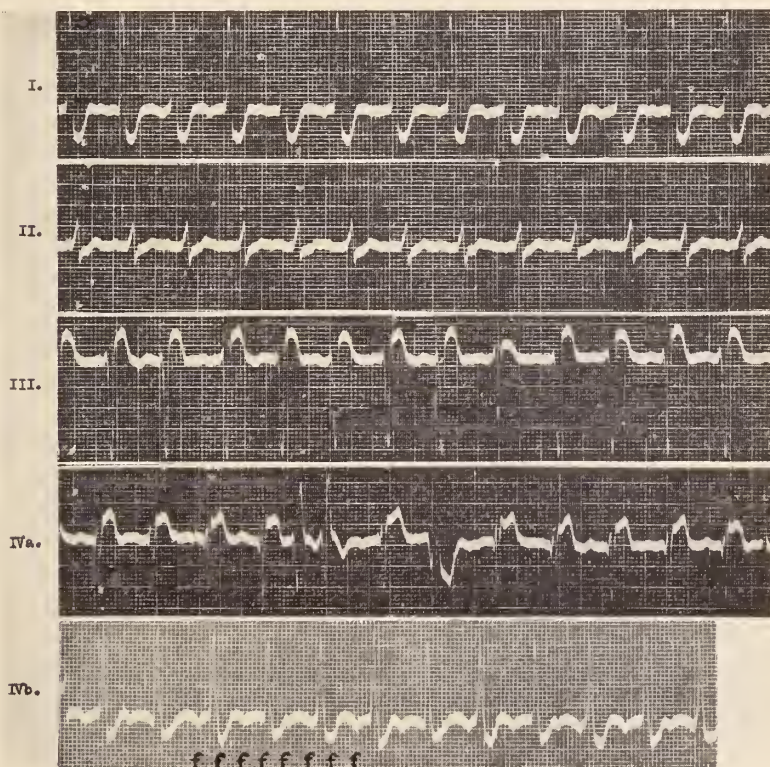
P. K., female, age 65.   Electrocardiogram, taken with three standard limb leads, I, II, III, and two chest leads, IVa, just within the apex, IVb, over the sternum, shows auricular flutter with complete auriculoventricular dissociation. The flutter waves, f, are most conspicuous in Lead IVb.   Auricular rate, 280, ventricular rate 115.   Occasional ventricular premature beats, left ventricular preponderance, and high voltage of the QRS complex are present.   The striking abnormality is the marked depression of the R-T segment in Leads I and IVb, and elevation in Leads III and IVa.   These changes are seen specifically in acute coronary artery occlusion.

calcified.   Dilatation and hypertrophy of the heart were also noted and sclerosis and ulceration of the aorta, chronic passive congestion of liver, spleen, kidneys, bronchopneumonia and multiple suppurative infarcts of the right lower lobe.   The coronary arteries were patent and there was no evidence of myomalacia.

COMMENT

Although the coronary arteries were patent and there was no myo-malacia, the syndrome of coronary thrombosis was closely simulated, even electrocardiographically. This is further evidence that the characteristic electrocardiographic changes of coronary occlusion, as well as precordial pain, are the result of ischemia of the heart muscle, and not of disease of the coronary arteries per se. In the case reported very little blood was permitted to pass through the pin-hole aortic valve. Consequently the blood flow through the coronary arteries was markedly reduced, producing ischemia of the myocardium. The latter was further increased by the presence of heart failure and tachycardia. Death occurred because of the continued insufficiency of blood flow to the heart despite the absence of acute injury to the heart muscle. The frequent finding of conduction defects in cases of calcareous aortic stenosis has been stressed by Boas. In our case complete heart block was associated with auricular flutter, a very unusual combination, which has been reported in the literature less than forty times. The arrhythmia was the result in this case, as usually, of extension of the calcification of the valve into the interventricular septum.

This case illustrates further the importance of rheumatic fever in cardiac disease even in the aged. The heart was involved presumably at an early age but in the absence of further attacks the patient lived to be 65 and, as not infrequently happens, carcareous deposits were engrafted on the diseased valve. In view of the severe degree of sclerosis of the aorta, it is probable that the calcification was part of a generalized process, superimposed upon a damaged valve.

Conclusion. It appears that both the characteristic clinical and electrocardiographic picture of coronary artery thrombosis are due in this case to ischemia of the heart muscle and not to acute myocardial damage. This is the first time an electrocardiogram characteristic of coronary thrombosis has been published in a case of aortic stenosis and collapse.

THE OCCURRENCE OF RHEUMATIC FEVER IN A PATIENT WITH RHEUMATOID ARTHRITIS

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In previous articles we have discussed non-specific acute polyarthritis and concluded that there were two types electrocardiographically, rheumatic fever and rheumatoid arthritis. These were frequently indistinguishable clinically except that the former involved the heart, while the latter did not. Thus we reported electrocardiographic changes in 100 per cent of cases of rheumatic fever when records were taken frequently, whereas in rheumatoid arthritis only minor changes occurred in a few cases. It is therefore important to differentiate the two from the standpoint of prognosis. Rheumatic fever is apt to produce permanent changes in the heart, whereas rheumatoid arthritis in many cases leaves residual deformities of the joints. From time to time reports of the simultaneous occurrence of both conditions in the same patient have appeared in the literature. The patient to be described possibly presents such a combination.

History (L. B., Adm. 391742). The patient was an unmarried female, twenty years of age. She was observed first at the age of eight suffering from chorea. Four years later the cycle of rheumatic fever continued with an attack of pericarditis with effusion, and the following year chorea recurred. At this time mitral stenosis and insufficiency and aortic insufficiency were well established. During the following years the patient suffered numerous attacks of migratory pain, tenderness and swelling involving the knees, ankles, elbows and wrists. These joints gradually became deformed and stiff. Similar changes later occurred in the small joints of the hands and fingers. For three years progressive curvature of the spine occurred. The patient entered the hospital because of pains in the knees and wrists for several months.

Examination. The patient was well nourished but appeared pale and chronically ill. The teeth were carious. There was bilateral ethmoiditis. All the superficial lymph glands were moderately enlarged. The chest was severely deformed by kyphoscoliosis of the lumbo-dorsal spine. The lungs were clear. The heart was enlarged to the left and a tachycardia and gallop rhythm were observed. Murmurs of mitral stenosis and insufficiency and of aortic insufficiency were present. The pulse was Corrigan in type. The blood pressure was 150 mm. Hg. systolic and 52 mm. Hg. diastolic. The elbows, right wrist, and both ankles were con-

siderably enlarged with limitation of motion at the joints. There was ulnar deviation and spindle-shaped deformity of the joints of both hands. The bones adjacent to the joints showed atrophic changes on teleoroentgenogram, as seen in rheumatoid infectious arthritis.

The hemoglobin was 59 per cent and the white blood count 7,200 with 69 per cent polymorphonuclear cells. The sedimentation rate was 26 minutes. The Wassermann reaction and blood culture were negative. The blood serum agglutinated streptococcus hemolyticus in 1:320 dilution and the blood plasma contained antifibrinolysins.

During the first two weeks there was a low grade fever and persistent tachycardia of 100–120 beats per minute. During the third week the temperature rose to 103°F. At this time a friction rub was heard over the precordium for several days and both ear drums were acutely inflamed.
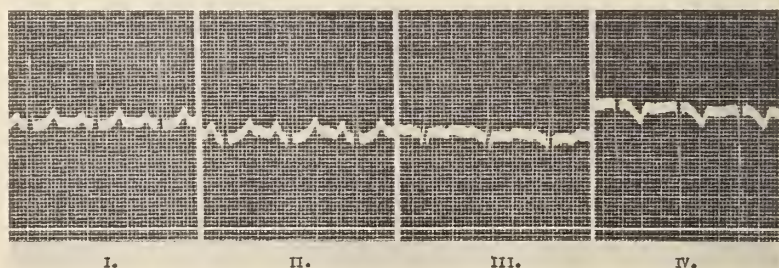
L. B., female, age 20. Sinus tachycardia, rate 90 beats per minute. P-waves large. Voltage of the QRS group high. R-T segment depressed in Lead II. T-3 inverted. The large P-waves suggest auricular enlargement and the high voltage without ventricular preponderance is seen when both ventricles are enlarged, as in this patient with mitral and aortic disease.

Improvement then was rapid and the temperature returned to normal and pulse rate became slower.

The electrocardiogram on admission showed sinus tachycardia, large P-waves, and high voltage of the QRS complex without ventricular preponderance. The T-wave in the third lead was inverted. Subsequent records showed minor changes in the R-T segments and T-waves.

COMMENT

If we consider rheumatic fever and rheumatoid arthritis separate entities, the course of the patient reported included several episodes of rheumatic fever until the age of thirteen, producing chronic cardiovalvular changes. This was followed by repeated attacks of rheumatoid arthritis with progressive deformity of the spine and joints of the extremities. Whether her symptoms on the last admission was those of a fresh attack of rheumatic fever or of rheumatoid arthritis was uncertain, in spite of the persistent

tachycardia and gallop rhythm, until a friction rub was heard.   We have never observed this in rheumatoid arthritis.

On the other hand there is again a tendency to consider rheumatic fever and rheumatoid arthritis as one disease; in some cases the heart is predominantly involved; in others, the joints and, very occasionally, both. In the terms of allergy, the shock organ varies.   However, even severe and prolonged inflammation of the joints in rheumatic fever is always followed by complete restitution.   The occurrence of definite joint deformities considered typical of rheumatoid arthritis in a patient with rheumatic disease, as in the case reported, is rare and probably no greater than in a control group.   The combination may be merely a coincidence.   A patient who has had attacks of rheumatic fever happens to develop a rheumatoid arthritis.   Until the etiology of both diseases is determined their relationship must remain uncertain.

Recently much has been written of the importance of the investigation of the blood antifibrinolysins and agglutinins against the streptococcus in the differential diagnosis of rheumatic fever and rheumatoid arthritis. However, as yet, the results are indefinite.

Conclusion.   A young woman has definitely suffered both from attacks of acute rheumatic fever and acute deforming rheumatoid arthritis.   In the episode described in this report there may have been a simultaneous occurrence of these conditions.

RENAL INFECTIONS*

EDWIN BEER, M.D.

The following remarks are limited to the common and more frequently seen types of infection of the upper urinary tract, excepting tuberculosis, actinomycosis and the like. In considering the bacillary and coccal infections, one includes the infections due to colon bacillus, bacillus pyocyaneus, bacillus proteus, bacillus Friedlaender, staphylococcus aureus and albus and streptococcus pyogenes and perhaps also hemolyticus.

The most frequent type of bacillary infection is due to the colon bacillus and the most frequent coccal infection is caused by the staphylococcus aureus. In the understanding of these conditions, it is gradually being appreciated that anomalies in the urinary tract play an important part, not only in the localization of the infection, but in the course of the disease. Modern urology can readily demonstrate by various methods the anatomical anomalies, but it is perfectly conceivable that there are physiological anomalies which, as yet, have not been demonstrated. Perhaps these physiological anomalies are just as important in the localization of the disease and its course as the anatomical alterations. Of recent years, attempts have been made by cinofluoroscopy to detect these physiological anomalies, but, as yet, the method is too expensive and its results are far from conclusive.

The distinction between the bacillary and the coccal infections of the upper urinary tract are absolutely fundamental and are not to be confused. Whereas the coccal infections are rarely associated with pyuria, unless the suppurative process bursts into the glomerulus or tubule, the bacillary infections are regularly associated with pyuria. In the coccal infections of the parenchyma the urine is usually absolutely clear, and microscopically may reveal a few red and white blood cells; while in the bacillary type a turbid urine discloses quite regularly on microscopic examination many clumped pus cells. Moreover, cultures of the sterilely obtained urine show in the bacillary type the various forms of bacilli referred to above, whereas in only a small percentage of the coccal infections does the urine yield a definite culture of staphylococcus or streptococcus. H. Cabot, basing his opinion on older and more recent studies made by himself and his associates, believes that in the rapidly centrifuged urine, smears will show cocci with great regularity. In our experience, and apparently also in that of many others, this proof of the presence of staphylococcus infection

of the kidney cortex has not been obtained.   In fact, in a recent series of cases, strangely enough, the few which showed the cocci on smear of centri- fuged specimens of urine were cases which had no renal cortical involvement. In one instance there was a perirenal abscess due to spinal tuberculosis and in another there was an abscess in the psoas muscle, simulating a peri- nephric abscess.   In all of the proven cases of cortical abscess no micro- organisms of the coccal type were found on smear.

The Bacillary Infections.   For many years there has been dispute as to the path of infection to the kidney in the bacillary cases.   For the longest time it was thought that such infections ascended in the urinary flow from the bladder through the ureter to the pelvis of the kidney.   This view was recently fortified by some animal experimentation and cystograms by a number of urologists in Boston who claim that they have observed very frequently a reflux of urine up the ureter to the kidney while the animal was being fluoroscoped under anesthesia.   Subsequently, they tried to apply this method of study to the human and claimed that, while doing cystograms, a ureteral reflux was also frequently observed.   As this was totally contrary to the experience in our institution, I had Dr. Aschner some years ago repeat this experiment on our material.   He was able to demon- strate that such refluxes up the ureter were a rarity and only occurred in definite pathological conditions of the wall and neck of the bladder.   The other channel of ascent, which was considered by many students to be responsible for the so-called pyelonephritis of the bacillary type, was the lymphatics.   This theory, however, in view of the anatomical arrangement of the lymphatic structures in the wall of the ureter, seems highly improb- able, as direct extension from the bladder or other pelvic viscera can hardly take place through these channels.   Moreover, recent experimental work has shown that, when india ink is injected into the wall of the bladder, the tendency is for the india ink to ascend via the lymphatics and to sweep up- wards towards the preaortic glands, and not in the direction of the ureter and kidney.   In some of the experimental data one may occasionally see a reflux of the india ink granules from the uppermost lymph nodes over the aorta back towards some of the vessels in and about the hilus of the kidney. It is conceivable that bacteria may enter by this route from below through the lymphatics into the lymph stream of the kidney, but the direct proof of this experiment or otherwise has not as yet been provided.

In general, one must believe that most of these bacillary kidney infec- tions, just as the coccal infections, are hematogenous.   I am fairly con- vinced that in the pyelonephritides the chill, which ushers in the hematog- enous infections, precedes the pyuria and the same sequence of events has been noted on one of the large obstetrical services abroad.   In other words, the bacillary invasion of the blood stream comes first, and, if a blood culture is taken during that period, it may show, in a considerable percentage of the cases, colon bacilli or any of the bacillary invaders.   Subsequently the

pyuria becomes manifest.   Usually during the chill there is a good chance
to pick up a positive blood culture.   In the Massachusetts General Hos-
pital the incidence of positive cultures has been well over 30 per cent, con-
siderably higher than we have been able to obtain in our institution.

As is well known, the coccal infections are definitely blood borne.   The
patient has a staphylococcus aureus or albus infection of the skin; in the
course of time the blood is invaded and emboli of cocci arrive in the cortex
of the kidney, resulting in the pathological picture.   There has always
been some question as to how these minute emboli traverse the pulmonary
circuit, and it has been thought for years that either the embolus arrives in
the right auricle and traverses an open foramen ovale, or it passes direct to
the lungs, where it produces a thrombophlebitis of the smaller venules.
From there the cocci are fed into the general circulation by the left ventri-
cle.   This view has been advanced by the Hamburg Pathological Institute,
but has not been confirmed as yet.   It would be highly useful to study this
very perplexing condition, particularly if an explanation of these general
systemic infections could be found in such localized pulmonary thrombo-
phlebitides.

Clinical Features.   The clinical picture of the bacillary infections includes
a great many variations in the pathological substratum.   Repeatedly,
inflammations of the bladder and ureter (cysto-ureteritis) produce a febrile
condition, simulating very closely the clinical picture observed in cases of
ureteropyelitis, or ureteropyelonephritis, so that without adequate study
it is often very difficult to know just where the infection begins or stops.
In children who have attacks of what was previously thought to be pyelitis
associated with pyuria, we often demonstrate the late effects of this disease
as being more marked in the ureter by finding a well developed dilatation
of this organ.   In other cases, we can demonstrate that the main disease
has been in the pelvis of the kidney by finding marked dilatation of one or
more calices, as well as of the pelvis.   During the acute stage, naturally,
this localization of the inflammation is not regularly possible.   In those
cases of acute pyelonephritis, in which there is frequently, though not reg-
ularly, well marked tenderness in the lumbar region over the involved kid-
ney, one occasionally has an opportunity either at autopsy or at operation
to see the havoc produced by these bacillary infections.   Under such cir-
cumstances, on decapsulating the kidney, one sees, scattered throughout
the cortex, many foci of suppuration, which on microscopic section can be
seen to be situated in the stroma between the tubules and the glomeruli,
as well as in between the tubules in the pyramids.   Naturally, with a dif-
fuse involvement of the parenchyma in this form of the disease, as op-
posed to the superficial mucous membrane infections, which are probably
just as common, one can readily understand why such a vast amount of
heterogenous data has been published concerning the various forms of
therapy and their results.   Over thirty years ago I was able to prove, at
least to my satisfaction, that the miliary foci of suppuration seen in the

protracted pyelonephritides resisted every effort to effect a cure of such diffuse involvement by drug therapy or by irrigation of the pelvis through the ureteral catheter. Apparently in these foci of suppuration the methylene blue and indigo-carmine are deposited in the leuco form, and I have been able experimentally in dogs to reproduce these blue stained abscesses, which only become blue on oxidation. At that time I saw a patient who had a colon bacillus infection of both kidneys and ran a high temperature. The late Dr. Edebohls wished to decapsulate both kidneys, but, as I understand it, Dr. Arpad Gerster, upon being called in consultation, gave a favorable prognosis if the patient were not operated upon. At that time methylene blue was one of the favorite urinary drugs, and it was administered to the patient for several months, her condition gradually improving and the temperature returning to normal. The lumbar distress disappeared, but the pyuria, as so regularly happens in this type of case, continued. About eight and a half months after the last dose of methylene blue was given, I was called in to catheterize the ureters in order to determine from which side the pyuria originated. During this study each voided specimen was saved in a separate bottle to see whether there were variations from urination to urination in the amount of the purulent sediment. Much to my surprise, marked variations in the deposit of pus were easily demonstrated, and, shortly after beginning the experiment, I noticed that one specimen of urine was definitely stained blue, although, when fresh, the pus at the bottom of the vessel was exactly of the same color as that voided in the specimens before and subsequently. Gradually, the purulent sediment became blue and began to color the supernatant, almost clear, urine. A chemical analysis made by a competent investigator, bore out the already surmised conclusion that we were dealing with methylene blue. This methylene blue had been given to the patient up to eight and a half months previously, and apparently had been stored in the parenchymal abscesses incidental to the acute pyelonephritis, then it had been discharged in the leuco form and, on oxidation, had produced the blue discoloration of the pus. This delayed excretion of methylene blue continued and the last specimen from this particular patient that was positive was two and three-quarters years after the oral administration of the methylene blue.

Indigo-carmine is regularly used in this institution as a functional test and fortunately, just as methylene blue, its late discharge can be watched in these pyelonephritic cases, as it also is deposited in the leuco form and, on standing, changes to the deep blue of indigo-carmine. These positive late excretions are of interest, though not a particularly valuable test, except that one can quite often recognize such late excretions and clarify thereby the clinical picture. On our service we have at each patient's bed at least one urine, which is more or less recently voided and we see occasionally such late excretion of indigo-carmine in these cases.

Treatment. As already mentioned, with such a parenchymal involvement, it would be difficult to attain a cure by therapy, such as by the

administration of antiseptics, urotropin, salol, pyridium, hexylresorcinal, acidifiers alternated with alkalies, acid diets, beta-oxybutyric acid or with mandelic acid in its various forms. All these therapeutic measures, as Dr. Brennerman at the Children's Hospital in Chicago recently stated in my presence, can only affect the simpler and more superficial infections. In the case of mandelic acid in particular, one of his assistants demonstrated a series of apparently improved patients with their pyuria fairly well controlled, but only as long as the mandelic acid therapy was continued. It is obvious that the important consideration, outside of the so-called bacteriostatic or bactericidal drugs, is to build up the patient's general resistance, and to correct any definite congenital anatomical, or possibly physiological, anomaly. In my experience in most of the simple, non-complicated and non-obstructed acute pyelonephritides, castor oil is almost a specific. Some of these very sick patients look on the fever chart as if they were in a sorry plight, but clinically look remarkably well, though they may be having chills two or three times a day. In these patients, apparently, there is an invasion of the blood stream from the more or less incompletely evacuated colon, and a liberal dose of castor oil, followed by a capsule containing castor oil min. V., and salol gr. V., four times a day has, in my experience during the last fifteen or twenty years with innumerable cases treated by this simple method, been followed by remarkably rapid improvement. Even in obstructed cases, caused by enlarged prostates, strictures, or stones in the kidney, it is worth while, in the face of complicating pyelonephritis, to try a dose of castor oil, as, even under these circumstances, it may act almost like a specific.

One of the most striking instances of the beneficial effect of castor oil was in a young woman who was subjected to all the most modern urological studies, as well as all the most modern forms of therapy. Her kidneys were catheterized and washed out, her bladder was also washed out, and, despite all this, she continued to run a high temperature with occasional chills and constant pyuria. There was no obstruction, the urinary tract was perfectly patent, but she had a persistent bilateral infection, which improved on catheterization of the ureters, but then, after a few days, relapsed with the return of fever, chill and pyuria. The patient was under treatment in this way for some eight weeks when she was brought under my care, and entered the hospital with a temperature of 104°F., and well marked pyuria. I asked her whether her bowels moved, and she answered in the affirmative. I asked if she had any cathartics during the last eight weeks, and she stated she had had an enema every day. She was given a large dose of castor oil, followed by castor oil and salol capsules, and within thirty-six hours her temperature had dropped to normal and the slight renal tenderness disappeared. Her temperature remained normal.

There are many other similar cases which have come under my care, and only a few years ago one such patient, with three shaking chills in twenty-four hours and temperature up to 106°F. was seen and treated in

this way, without any preliminary X-ray examination, which she refused to have. Here also, within thirty-six hours the temperature dropped to normal, so that she was able to be up and about within a few days following this regime. Indeed, she still had, as they are liable to have, chronic pyuria until the multiple foci of suppuration had been discharged into the urinary tract.

In some of the most violent cases of bacillary infection, it may be necessary, even in the absence of stone or obstruction, to expose the kidney and to decapsulate. Apparently such kidneys following decapsulation, whether the operation was or was not indicated, do rapidly improve and the general condition of the patient within twenty-four hours shows a marked change for the better. This applies particularly to those cases of bacillary infection associated with diabetes, as the diabetic kidney seems to have difficulty in taking care of the infection within the dense capsule which surrounds the cortex of the kidney. In diabetic cases with these colon bacilli or other bacillary infections, owing to the formation of definite liquefying abscesses, a rare case presents itself in which a nephrectomy has to be carried out.

Coccal Infections. Opposed to the bacillary infections which regularly show pyuria, are the infections of the coccal group, which are associated with perfectly clear urine and microscopically may show a few red blood cells at the inception and only occasionally show some pus cells as the abscess or furuncle ruptures into the tubules. In a considerable number of these coccal infections, which arise from skin lesions, gum boils, tonsillitis, upper respiratory infections and the like, the blood culture may at times be positive, then may become sterile and afterwards positive again. Also the urine may show cocci in culture and, as mentioned above, according to some clinicians, smears from the centrifuged urine may show similar organisms. The clinical picture of these cases is quite different from the bacillary infections. These patients almost invariably have local pain, whereas there are many cases of silent bacillary pyelonephritis. They may complain of lumbago, usually run a temperature, have jar tenderness over the involved kidney with rapid loss of weight and show a well marked blood picture of infection. In addition, the X-ray studies of the urinary tract give very helpful data which I emphasized a few years ago. It had been known for years that large kidney masses, hydronephroses, tumors and perinephric abscesses, if sufficiently opaque, can obscure the margin of the psoas muscle. It had also been noted by orthopedists that in cases of psoas spasm there was a tendency of the spine to curve away from the lesion. These two signs, commonly seen in perinephric abscess, which is practically always secondary to a cortical furuncle or carbuncle, I found of great significance in the diagnosis of cortical coccal infections, but it is absolutely essential when establishing the value of these signs to prove that the involved kidney is not blocked, that it is secreting clear urine and that the pyelographic data exclude hydronephrosis or neoplasm. Unless one is

certain that such a kidney is not blocked, one may find the roentgenological signs of a perinephric abscess secondary to a cortical abscess in patients with either large neoplasms, which are infected or non-infected, or with infected hydronephroses or pyonephroses. Another help in the diagnosis of these conditions, which, at times, may be very obscure, are the pyelographic data which may mimic very closely the deformities produced in the calyces that one sees in cysts or neoplasms of the kidney.

As far as therapy in the cortical coccal furuncles or carbuncles is concerned, usually operation becomes necessary, although occasionally one sees cases which have the typical clinical picture and are spontaneously relieved. In the great majority of cases, however, the furuncle or carbuncle ruptures into the perinephric space and produces an abscess, which has to be drained. If one operates early, one can often recognize the cortical lesion of the kidney following decapsulation, even without delivering the organ freely in the wound. In old perinephric abscesses, naturally, the exudate binds the kidney in position, so that one is unable to make a complete inspection of the kidney cortex. All furuncles or cortical kidney coccal infections should be opened after decapsulation and thoroughly drained. Should one encounter one of the larger suppurative foci, corresponding to that which one sees in carbuncles of the neck, some time after the third week, one can enucleate bluntly with the handle of the scalpel or with one's finger all of the suppurative infarct and pack the opening after the removal of the wedge shaped necrotic mass of kidney tissue. Conservative surgery in these cases is strictly indicated, as the process, in view of its hematogenous character, may prove to be bilateral, as I have seen a number of times, and nephrectomy of the first kidney may be fatal to the patient's life.

In closing let me again emphasize,

1. that there are very definite differences between the bacillary and coccal infections of the kidney;

2. that a study of the pathology, as illustrated in the cases operated upon and those that come to autopsy, and by the study of the late excretion of methylene blue and indigo-carmine, leads one to an understanding of why the various antiseptic drugs and diets fail to regularly cure the really severe cases of pyelonephritis, whereas it is perfectly understandable how these various bacteriostatic and bactericidal agents may be curative in the surface involvement of the mucous membrane of the bladder, ureter and pelvis of the kidney;

3. that operative treatment of the bacillary type of infection of the kidney is rarely required, whereas in coccal infections of the parenchyma of the kidney, operative treatment is usually essential;

4. that in the acute bacillary infections of the kidney, the most efficient treatment, which seems to behave almost as a specific, is castor oil in adequate doses, followed by capsules of castor oil and salol.

CLINICAL PATHOLOGICAL CONFERENCES

GEORGE BAEHR, M.D., AND PAUL KLEMPERER, M.D., *presiding*

Wednesday, March 10, 1937

Case 1. Periarteritis Nodosa: The Relationship of Allergic Phenomena, such as Asthma, Urticaria and Eosinophilia

(From the Medical Service of Dr. George Baehr)

History (Adm. 402614).   The patient, a white housewife, entered the hospital complaining of asthmatic attacks of sixteen months' duration, progressive weakness, loss of weight of six months' duration, and since the onset of her complaints attacks of dyspnea, sweating and cyanosis.   The asthmatic attacks were severe enough to necessitate several periods of hospitalization.   During the past six months she had had a rather persistent diarrhea, consisting of four or five loose, non-bloody bowel movements each day.   Four months before her admission to The Mount Sinai Hospital she entered another hospital where a left deltoid biopsy disclosed the presence of periarteritis nodosa.   Following this procedure she developed weakness of that extremity and a wrist drop.   Shortly thereafter, her vision became impaired and epigastric pain appeared, unrelated to food, time, exertion or bowel habit.   She lost approximately fifty pounds during the past year.   For the two weeks prior to her hospitalization she suffered with episodic bouts of dyspnea, cyanosis and diaphoresis, dysphagia and vomiting.   There had been no urinary symptoms.

Her family history is interesting in the respect that one sister died in 1934 of a diffuse vascular disease.

Examination.   The patient was a poorly developed, cachectic, pallid female, irrational, confused and disoriented with moderate cyanosis of the lips and finger nails and engorgement of the neck veins.   The fundi were pale; the discs, atrophic. The retinal arteries were thin.   A small hemorrhage was found above the right disc.   A few small lymph nodes were palpable in the posterior triangles of the neck, axillae, epitrochlear regions and groins.   There was slight dulness at the right base posteriorly with numerous moist and crackling râles.   Similar râles were audible over the right upper anterior chest and over the left base.   The heart was slightly enlarged to the left on percussion.   Sounds were of fair quality; gallop rhythm and a grating systolic rub were heard to the left of the lower end of the sternum. The liver was tender; its smooth edge extended to a point two fingers' breadth below the umbilicus.   The spleen was not palpable.   There was a small movable subcutaneous nodule of cartilaginous consistency on the lateral aspect of the right knee, and a somewhat larger nodule over the tenth dorsal spine.   Slight pitting edema of the ankles was present.

There was a wrist drop and median nerve paralysis of the left hand.   The fingers were held in adduction with flexion of the proximal interphalangeal joints.   The patient was unable to abduct fingers and thumb.   There was some hyperesthesia of the dorsum of the left hand.

Laboratory Data. The blood pressure was 150 systolic and 110 diastolic. The hemoglobin was 83 per cent, red blood cells 4,430,000; white blood cells 19,250 per cu. mm. with 91 per cent polymorphonuclear leucocytes, 2 per cent eosinophiles. The blood urea nitrogen was 75 mgm. per cent, sugar 75 mgm. per cent, uric acid 6, calcium 9.5, phosphorus 3.2, cholesterol 165, chlorides 525. The blood CO_2 was 25 volumes per cent. The urine revealed a faint trace of albumin and concentrated to 1028. The urinary sediment revealed an occasional erythrocyte and few white blood cells. The temperature was subfebrile with a preterminal rise to 104.0°F.

Course. The patient remained disoriented with only occasional periods of lucidity. She went downhill very rapidly and died nine days after her admission, sixteen months after the onset of her complaints.

Necropsy Findings. Evidence of periarteritis nodosa was revealed with involvement of the vessels of the kidneys, liver, mesentery, diaphragm, spleen, lungs and
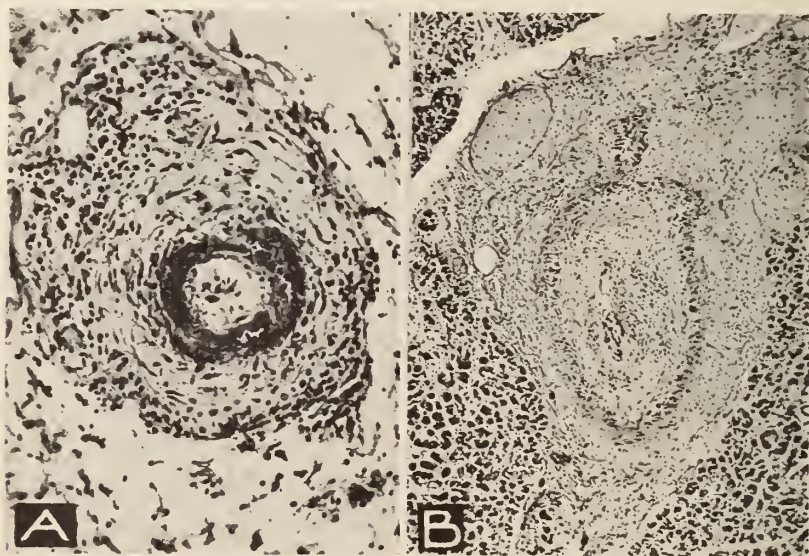
Fig. 1 (Case 1). A. Acute necrotizing arteritis in epicardium. B. Fibrosing arteritic lesion in pancreas.

heart. There were diffuse cortical scarring of both kidneys and subcapsular atrophy of the liver. The heart was moderately enlarged and its chambers dilated. The myocardium showed disseminated areas of fibrosis. There was a recent extensive suppurative pericarditis. There were also anasarca, passive congestion of the lungs and liver, a hemorrhagic infarction of the right lower lobe and an extensive bronchopneumonia. Death was attributed to bronchopneumonia and cardiac failure.

Comment. Dr. Klemperer emphasized the point that it is the artery of small calibre which is notably affected in the disease process referred to as periarteritis nodosa. The apparent increase in the incidence of the disease was believed to be due to the fact that the microscopic picture of the disease has recently been studied more assiduously and relied upon.

Dr. Baehr raised the question of the occurrence of asthma in this patient and

alluded to the various allergic manifestations which were observed during the course of this disease. Eosinophilia is commonly observed in cases of periarteritis nodosa. Although it was not present during the terminal stage of the disease, it had been observed during the first hospital admission. In a woman with this disease, who is now under observation in the Semi-Private Pavilion of the Hospital, an eosinophilia of 50 per cent has persisted for four months. The vascular disease was preceded by three weeks of intractable urticaria of undetermined origin.

Dr. Baehr also discussed the occurrences of prolonged remissions and even possible recoveries in this condition. He recalled a patient, seen some years ago, in whom the vascular lesions had evidently cleared up, but who had ultimately succumbed to the onset of a renal insufficiency, possibly the consequence of a diffuse replacement fibrosis.

An excellent review of the subject of periarteritis nodosa was recently published by Dr. Rose Spiegel in the Archives of Internal Medicine, (Clinical Aspects of Periarteritis Nodosa, 58: 993, 1936).

Case 2. Addison's Disease Complicated by Acute Cholecystitis: A Problem in Therapy

(From the Medical Service of Dr. George Baehr and the Surgical Service of Dr. Richard Lewisohn)

History (Adm. 399938). The patient, a 44 year old American born male, was first admitted to The Mount Sinai Hospital in October 1936 because of weakness of one month's duration. Twenty-six years ago (1910) he had spent four years in a sanatorium because of a chronic cough, night sweats and a sputum positive for tubercle bacilli. He was finally discharged as an arrested case. Thereafter he was constantly afebrile but after his discharge continued to have a chronic morning cough, productive of a small quantity of thick viscid sputum. A short time after his departure from the sanitorium he had a small hemoptysis. His weight was steadily maintained, however. In May 1936, five months before admission, he was suddenly seized with severe upper mid-abdominal pain, associated with vomiting. The pain was steady in character, did not radiate and lasted about twenty-four hours. At that time his attending physician made the diagnosis of gall-bladder disease but also noted cutaneous pigmentation. One week later he experienced another episode of upper abdominal pain which was similar in character and duration to the previous attack. There were no chills, fever, jaundice, diarrhea, clay-colored, bloody or tarry stools. For the six months prior to his admission he had been moderately constipated and experienced gradual loss of libido, strength, and occasional cramp-like pains in his legs. He lost twenty pounds during this period. There had been no recent increase in the pigmentation of the skin.

Examination. The patient appeared chronically ill, asthenic. There was a diffuse brown pigmentation of his skin which was more pronounced in the exposed parts, and an intense brown pigmentation of the lower lip and buccal mucous membrane near the angles of the mouth. There was slight dulness over both supraspinous fossae and in the left infraclavicular fossae and harsh breath sounds with occasional dry clicking râles over these areas. The remainder of the physical examination was negative.

Laboratory Data. The systolic blood pressure was 86 mm. of mercury and the diastolic, 64. The hemoglobin was 89 per cent; the white blood cells 7,900 with 56 per cent polymorphonuclear leucocytes. The erythrocyte sedimentation time was over four hours. The urinalysis and blood Wassermann reaction were negative; the blood urea 32 mgm. and glucose 90 mgm. per 100 c.c.; sodium 126 milliequivalents (normal 140 milliequivalents per liter), chlorides 93.4 milliequivalents (normal 98–106 milliequivalents per liter). The Janney test showed a maximum blood sugar of 150 mgm. per 100 c.c. An X-ray examination of the abdomen failed to reveal any calcification of the adrenal glands. The diagnoses entertained were chronic bilateral fibrocaseous pulmonary tuberculosis with tuberculosis of the adrenal glands (Addison's Disease). Except for a rise of temperature to 100.8°F. on one occasion the patient remained afebrile during his entire stay of four and a half weeks.

On a high salt intake dietary regime, he showed rapid gain in strength and weight (ten pounds). His systolic blood pressure rose to 112 mm. of mercury and the diastolic, 76. The blood sodium, however, did not rise to the height which it usually reaches in a remission and did not exceed 133 milliequivalents. Before his clinical improvement he was discharged to the care of his private physician on October 19, 1936.

Second Admission. He was readmitted on February 3, 1937. Since his discharge the patient had been taking 15 grains of sodium chloride each day and had been rather well. Two days before admission, however, he suffered a sudden onset of severe aching epigastric pain which radiated toward the right upper quadrant. The pain was steady and continued to the time of his admission and was associated with anorexia. The morning of admission, nausea and vomiting of greenish material appeared, with feverishness and mild chilly sensations. There had been no jaundice.

Examination. In addition to the findings previously noted, there were moderate direct and rebound tenderness in the right upper quadrant with rigidity. The patient's temperature was 101.8°F., pulse 92 per minute. The white blood count was 16,000 per cu. mm. with 78 per cent polymorphonuclear leucocytes. His urine was negative. During the next forty-eight hours the temperature reached 103.6°F. and his pulse rose to 130 per minute. The local signs became more marked and it was then deemed advisable to operate. It was clinically obvious that the patient had an acute cholecystitis. Gangrene of the gall-bladder was feared unless the spreading infection was operated upon and drained.

Laparotomy revealed an acutely inflamed gall-bladder but no biliary calculi. A cholecystostomy was performed. The postoperative condition was from the outset most unfavorable. He rapidly sank into a state of profound shock from which he could not be aroused in spite of intravenous injections of large amount of hypertonic as well as physiological saline solution, adrenal cortical extract, adrenalin and ephedrine. He ceased twenty-four hours following operation.

Necropsy Findings. The upper lobe of the right lung was firm, dense, shrunken and was adherent to the middle and lower lobes through fibrous adhesions. On section the bronchi were found dilated, their mucosae granular, reddened. There was evidence of healed tuberculosis of the apex. The left upper lobe, on section, similarly showed a saccular bronchiectasis and a fibrocaseous apical lesion. There was a partial adhesive pleuritis of the left lung. The adrenal glands were moder-

ately enlarged, nodular. On cut section the basic structure of the glands was completely replaced by grey-yellow amorphous, partly caseous material. The gall-bladder was the seat of an acute, phlegmonous inflammation. There were also a localized acute fibrinopurulent peritonitis on the inferior aspect of the right liver lobe and marked parenchymatous degeneration of the heart and kidneys. The cause of death was attributed to acute adrenal insufficiency.

Dr. Baehr emphasized the difficult therapeutic problem which this case presented. Patients with Addison's disease offer an extremely poor operative risk. Almost invariably they die of surgical shock when subjected to any major operative interference. Some of the internists felt that the patient's chances would be better if he were not operated upon. However, under the influence of the increasing infection of the gall-bladder and a beginning local peritonitis, the Addison's disease was becoming rapidly uncontrollable, in spite of intravenously administered hypertonic salt solution and a potent cortin preparation. Death seemed inevitable unless the infection could be controlled. With full appreciation of the gravity of the risk, cholecystostomy was therefore performed as rapidly as possible.

In diabetic patients who develop intraabdominal suppuration experience has shown the wisdom of draining the suppuration without delay. After the operation the diabetes is much easier to control. If operation is delayed and the infection permitted to continue, the diabetes becomes rapidly more severe and more difficult to correct even with enormous amounts of insulin. The presence of a suppurating infection has a similar influence in Addison's disease and the operation was performed on the basis of this experience, although with little hope of success.

<div align="right">Wednesday, March 17, 1937</div>

Case 1. Perforated Adenocarcinoma of the Colon. Cylindrical Dissecting Aneurysm of the Aorta, "Double Barrel Aorta" (A Casual Post Mortem Finding)

(From the Surgical Service of Dr. Ralph Colp)

History (Adm. 404748). The patient, a 47 year old Negro janitor, entered the hospital complaining of abdominal pain of two days' duration. The onset of pain was sudden, colicky, periumbilical with gradual radiation to the right lower quadrant. There was no nausea, vomiting, chills or genito-urinary symptoms although "marked feverishness" was present from the onset. It is noteworthy that his past history was negative except for pneumonia and gonorrheal urethritis in 1922.

Examination. The patient was a very well developed, well nourished Negro. The left cardiac border extended to the left anterior axillary line at the level of the seventh rib. There were no murmurs. The blood pressure was 220 systolic, and 140 diastolic. There was moderate spasm and exquisite tenderness in the right lower abdominal quadrant. There was no abdominal distension; no masses.

Course. The blood Wassermann and urinalysis were negative. The patient was explored because it was thought that he had an acute gangrenous appendicitis with abscess formation. During the appendectomy the retroperitoneal tissue in the region of the ascending colon was found indurated, and the wall of the colon in this area was the site of a mass. Although a perforated carcinoma of the colon was suspected, it was considered inadvisable to subject the patient to further surgical manipulation at this time; the abdomen was closed with drainage.

The patient's postoperative course was stormy from the onset. His temperature, which was 99.2°F. on admission, rose to 105°F. on the day following operation. It remained at this level on the second day and was accompanied by chills and singultus. The wound became reddened and tender, the abdomen spastic. Removal of sutures resulted in the liberation of some purulent material, but the abdominal distension continued. Temperature fluctuated from 100° to 103° or 104°F. Ten days following admission, swelling, tenderness and induration were

Fig. 1 (Case 1). Syphilitic mesaortitis. Dissecting aneurysm of aorta involving pars descendens and left common and external iliac arteries. Stenosis of isthmus of aorta. So-called double-barreled aorta.

noted in the right flank. The same day the patient eviscerated several inches of small intestine and died twenty hours thereafter.

Necropsy Findings. The noteworthy findings were a small ulcerating adenocarcinoma of the ascending colon which had perforated into the retroperitoneal tissue and produced an extensive phlegmon. The inflammation had then progressed anteriorly and medially to involve the peritoneal cavity. There was evidence of an acute diffuse fecal fibrino-purulent peritonitis. The appendix removed at operation showed partial obliteration of its lumen. A very interesting and

surprising finding was a syphilitic mesaortitis with perforation of the inner coats at the isthmus and a dissecting aneurysm which involved the descending aorta, left common iliac and external iliac arteries (double barrel aorta). The heart was found markedly enlarged, and, more particularly, the left ventricular wall.

Comment: Dr. Baehr pointed out that dissecting aneurysms of the aorta are more commonly the result of arteriosclerosis rather than of luetic aortitis, as in this case. It is remarkable that the patient gave no history of illness or pain to mark the occurrence of the original rupture of the aorta months or years ago.

Case 2. *Lymphosarcoma with Chief Involvement of the Spleen*

(From the Medical Service of Dr. B. S. Oppenheimer and the Surgical Service of Dr. Edwin Beer)

History (Adm. 404030). The patient, a white female, aged 45, was first admitted to The Mount Sinai Hospital on December 22, 1936, complaining of sharp steady pain to the left of the umbilicus of ten weeks' duration, with radiation to the left costovertebral region. The pain was usually aggravated by food, exertion and deep inspiration. Since the onset of her complaints there had been a loss of weight of thirty-five pounds, but no anorexia, fever, chills, constipation, diarrhea or any urinary symptoms. There was also a history of a cholecystectomy in 1930 and a cardiac murmur for the past seventeen years associated with dyspnea on moderate exertion. There was no previous history of rheumatic fever.

Examination. The patient was a chronically ill female. The left heart border was moderately enlarged to the left. A loud harsh systolic blow was audible over the entire precordium with maximum intensity over the aortic area. The second aortic sound was equal in intensity to the second pulmonic sound. There was slight tenderness and rigidity over the left upper abdominal quadrant with punch tenderness over the lower ribs and left axillae. There was no significant lymphadenopathy.

Laboratory Data. A roentgenogram of the colon showed displacement of the splenic flexure downwards and medially by what was believed to be a mass in the region of the spleen. A gastro-intestinal series revealed no organic lesion in the stomach or small intestine but again evidence of a mass in the left upper quadrant which displaced the stomach to the right. A pneumo-peritoneum X-ray examination was inconclusive in defining the nature of the mass. A roentgenogram of the chest showed pleural thickening over the base of the right lung and evidence of a large left auricle. An electrocardiograph indicated the presence of left ventricular hypertrophy and some myocardial damage. An intravenous pyelogram revealed no abnormalities. The hemoglobin was 83 per cent; white blood count 14,000 per cu. mm. with 76 per cent polymorphonuclear neutrophiles, 23 per cent lymphocytes, 4 per cent monocytes, 3 per cent eosinophiles, and 1 per cent basophiles.

Course. The patient had a febrile course, her temperature occasionally rising to 102°F. with gradual defervescence to the time of discharge. In view of the clinical findings it was felt that there was a cystadenoma of the pancreas or a carcinoma of the tail of the pancreas. Operation was advised but refused and the patient was discharged on January 10, 1937.

Second Admission. After discharge from the hospital, the pain persisted but varied in intensity. There was an additional complaint of pain in the left shoulder.

On readmission (January 29, 1937) the physical findings were essentially the same as on her discharge. Two days later, however, signs of fluid appeared at the left base. Aspiration of the left pleural cavity yielded 25 c.c. of a turbid yellow fluid which contained 2,300 white blood cells, 4,500 erythrocytes. No organisms were found. The blood hemoglobin was 80 per cent; white blood count was 16,000 per cu. mm. with 88 per cent polymorphonuclear leucocytes, 7 per cent lymphocytes, 3 per cent monocytes and 2 per cent eosinophiles. Laparotomy disclosed a mass

Fig. 2 (Case 2). Lymphosarcomatosis with chief involvement of spleen. Extension to splenic flexure of colon.

the size of a large grapefruit which was found adherent to the left parietal peritoneum. The spleen could not be visualized and it was questionable whether the mass involved the spleen. During the attempt to separate the mass from the lateral abdominal wall, an abscess cavity was entered and a few drams of thick yellow purulent fluid were evacuated. Drains were introduced and the abdomen closed with layer suture.

Course. The patient did very poorly following this procedure, gradually but

steadily lapsed into coma and became distended.   She died on the tenth day of her second admission, thirteen weeks after the onset of her complaints.

Necropsy Findings.   The most noteworthy post mortem finding was a primary lymphosarcoma of the spleen, with extension through the splenic flexure of the colon and involvement of the diaphragm.   The splenic flexure of colon, the greater gastric curvature, the anterior and lateral surfaces of the diaphragm were stoutly adherent to the lower two-thirds of the spleen.   At the point of adhesion of the splenic flexure the colonic mucosa presented an ulcer 1 cm. in diameter.   This consisted of a slightly raised soft fleshy border and a grey shaggy base which was the site of a perforation.   The latter led to some granular and amorphous material over the lower pole of the spleen.   The spleen on section showed a replacement of its lower two-thirds by smooth uniform yellowish white tissue and scattered similarly colored, one-half to one cm. in diameter nodules throughout the remaining pulp.   There was also involvement of the peripancreatic, inguinal and mediastinal lymph nodes. Additional findings were a hemorrhagic pleural effusion with compression of the left lower lobe and to a lesser degree of the left upper lobe.   The heart revealed evidence of an organized rheumatic inflammation with valvular deformities consisting of an acquired bicuspid aortic valve with aortic stenosis and insufficiency, a mitral valvulitis with mitral stenosis and insufficiency, and a moderate degree of ventricular hypertrophy.   There were also multiple fibromyomata of the uterus and a thickened gall-bladder with biliary calculi.

The predominant involvement of the spleen justified the diagnosis of lymphosarcoma of the spleen in this case, although the morbid process was not limited to this organ, but had involved several lymph node regions.

Comment.   Dr. Klemperer remarked on the rarity of true primary lymphosarcoma of the spleen as opposed to the type which is the result of metastatic colonization in generalized lymphosarcomatosis.   In the so-called primary type the tumor formation has been reported to exist in the form of either one or more discrete masses or has produced a diffuse enlargement of the entire organ, occasionally with involvement of the regional lymph nodes.   In the metastatic varieties one or more sharply circumscribed small to cherry-sized foci may occur within the spleen.   Lymphosarcomatous foci in generalized lymphosarcomatosis, however, infrequently develop locally within the spleen as part of a systematized process affecting lymphatic tissue.   Thus in a series of 19 cases of generalized lymphosarcomatosis reported by Ehrlich and Gerber (Am. J. Cancer 24: 1, 1935) two such instances were described in which the splenic follicles contained atypical lymphoblasts with hyperchromatic nuclei.

Reported by Henry Horn, M.D.

ABSTRACTS

Members of the hospital staff and the out-patient department of The
Mount Sinai Hospital are invited to submit for publication in this column
brief abstracts of their articles appearing in other journals.

*The Treatment of Gonorrheal Arthritis by Means of Systemic and Additional Focal
Heating.* W. Bierman and C. Levenson. Am. J. M. Sc. 191: 55, January 1936.
Sixteen selected cases of gonorrheal arthritis are reported. These cases all had
received previous genito-urinary chemotherapy, intravenous vaccine or foreign pro-
tein or other medications for systemic reactions, and local joint orthopedic measures
without success. All had severe forms of arthritis before heat therapy. Each re-
ceived systemic temperatures of 105° to 106°F. for six hours and pelvic temperatures
of 109° to 110°F. for three to five hours. All were permanently cured of gonorrhea,
although in the males some required a short course of genito-urinary treatment. All
had complete restoration of function except two that came with bony ankylosis. To
speed restoration, measures to increase mobility and circulation of joints were also
used. Cases were followed up for from five months to two years with smears, com-
plement fixation, sedimentation rates and X-ray examination. The authors advo-
cate the early use of the treatment described as the best available means of prevent-
ing deformities and clearing up the foci of infection.

*Paralysis of the Axillary (Circumflex) Nerve with Spontaneous Recovery after Seven
Months.* S. Hirsch. J. A. M. A. 106: 705, February 1936.
The unusual etiology of paralysis of the axillary (circumflex) nerve is the subject
of this report.
A young girl, aged 14 years, was accidentally thrown off her horse. A fracture of
the acromial end of the right clavicle and comminuted fracture of the right scapula
were found and verified by roentgen studies.
At the end of the fifth week after injury, it was observed that the patient could
not actively abduct her right shoulder and exhibited paralysis of the axillary nerve
causing motor loss, atrophy of the right deltoid and analgesia over the cutaneous dis-
tribution of the axillary nerve.
With the arm in airplane position and with almost daily sinusoidal treatment,
gentle massage, manipulation and hot and cold contrast baths, first sensory return
and then motor return gradually appeared seven months after injury.

Recent Advances in the Surgical Treatment of Chronic Duodenal Ulcers. R. Lewisohn.
J. A. M. A. 106: 684, February 1936.
The vast majority of duodenal ulcers are situated in the first part of the duodenum
and should be treated by partial gastrectomy. When proper judgment is used in
the selection of the cases, the mortality is low. The author's mortality is 2 per cent.
In the very deep duodenal ulcers, Finsterer's prepyloric or postpyloric resection is
preferable to gastro-enterostomy. The judicious choice of partial gastrectomy

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(Billroth II) for the surgical treatment of duodenal ulcers has reduced the incidence of gastrojejunal and jejunal ulcers from 34 per cent to 7 per cent.

Recurrent Herpes Zoster (Femoralis); Report of a Case with Unusual Features. A. SAYER. Arch. Dermat. & Syphil. 33: 348, February 1936.

A case of recurrent herpes zoster is reported in a man, 74 years old. It is of interest because of the following:

(1) Recurrences of herpes zoster are rare.

(2) The eruption in this case occurred on opposite sides (a bilateral eruption).

(3) The lesions were hemorrhagic and surrounded by zones of intense redness, but neither necrosis nor scars followed.

(4) The patient did not take any drugs, nor did he receive any spine injury before the onset of these attacks.

Subphrenic Collection of Lipiodol following Injection into the Fallopian Tube; with Observations on Reverse Gravitation of Pelvic Exudates and the Genitophrenic Syndrome in Women. I. C. RUBIN. Am. J. Obst. & Gynec. 31: 230, February 1936.

The author collates his observations on the upward "gravitation" of infective and non-infective fluids from the pelvis toward the diaphragm based upon three points of view: (1) Clinical study of gonorrheal salpingitis and early and advanced ectopic pregnancy, (2) behavior of the CO_2 gas following uterotubal insufflation, and (3) the actual radiographic demonstration of lipiodol under the diaphragm following its injection into the fallopian tube. The clinical symptoms occasioned by the reverse gravitation of fluid exudates arising from the female genitalia and referred to the diaphragmatic area as well as to the shoulder are designated by the term, genitophrenic syndrome in women.

The Auriculotemporal Syndrome; with a Suggestion Regarding Therapy. W. NEEDLES. Arch. Neurol. & Psychiat. 35: 357, February 1936.

Following an operation for a tumor of the parotid gland, the patient developed a fistula. When this fistula was obliterated by the application of a caustic, the auriculotemporal syndrome appeared. Whenever the patient ate, profuse sweating occurred over the right side of the face in the distribution of the auriculotemporal nerve. In addition, there was diminution of pain, touch, and temperature sensation in this area. Pharmacodynamic tests indicated that the sweating phenomenon was due to stimulation of parasympathetic fibers. It was thought that during the act of eating, the parotid gland became enlarged and produced pressure on these fibers. Radiotherapy was applied to the parotid gland and effected an amelioration of symptoms. It could not be continued because of lack of coöperation on the part of the patient.

The Electric Charge of Mammalian Red Blood Cells. H. A. ABRAMSON AND L. S. MOYER. J. Gen. Physiol. 19: 601, March 1936.

From the data on the surface area and electrical mobilities of red blood cells in a given solution under approximately physiological conditions, the net surface charge per cell as well as the charge per unit area can be calculated by means of the modern theory of electrolytes. The lowest value of the net charge density in the series investigated was 1890 electrostatic units in the rabbit. Man and the rhesus monkey were the same, both having approximately 4500 electrostatic units of net charge per square centimeter. Amongst the mammals investigated, given here in the order of increasing charge density, were: rabbit, sloth, pig, opposum, guinea pig, man, rhesus monkey, cat, mouse, rat, dog; the dog had the highest charge density of 5600 electrostatic units. This order is completely changed if the effective number of electrons at

the surface of the cell, rather than the charge density, is calculated because this depends upon the size of the cell. Man, among the animals studied, had the highest number of effective electrons at the surface, the value being equal to 15 million electrons. In cases of anemia in human beings, the abnormal cells apparently possess a mechanism which is capable of keeping the surface density of net charge constant even though comparatively large changes in the surface area may occur.

Primary Carcinoma of the Extremities. E. M. BICK. Ann. Surg. 103: 410, March 1936.

This report is part of a general clinical study of soft-tissue tumors of the skin of the extremities. It relates particularly to primary carcinoma of the extremities, and emphasizes the possibility of early clinical presumptive diagnosis. These tumors represent approximately 5 per cent of all soft-tissue tumors of the extremities. Twenty-one cases were studied. Contrary to those previously reported, they were evenly divided between the sexes. In no other soft-tissue tumors of the extremities is the relationship between trauma and tumor so evident. The trauma may be direct or indirect. Heretofore, these tumors were considered to be associated predominantly with burn scars, but in the present series, association with old draining sinuses or old infected ulcers was equally frequent. In none of the cases was the ulcer of varicose origin. The age of onset ranged from 13 to 73 years. Carcinoma, unlike other soft-tissue tumors of the extremities, is frequently accompanied by pain. It should become a surgical axiom that the appearance of pain in an ulcer or sinus on an extremity, after a period of apparent quiescence, marks the onset of malignancy unless otherwise proven by careful biopsy. Except in melanocarcinoma, metastases occur late. With a few exceptions, primary carcinomata are the only soft-tissue tumors of the extremities which metastasize by way of regional lymph nodes. In general, the following treatment has been most successful: when only a digit is involved, immediate amputation should be performed; in other instances, wide excision through normal tissue followed by radiation is the procedure of choice; in advanced or recurrent cases, amputation followed by radiation of regional glands is recommended.

Extrasystoles of Clinical Significance. E. BOAS AND H. LEVY. Am. Heart J. 2: 3, March 1936.

At times the origin of extrasystoles is clear, as when they are caused by tobacco, coffee, or digitalis intoxication. Extrasystoles occurring at the onset or during the course of acute infectious disease indicate cardiac involvement, but not necessarily irreversible cardiac damage. Auricular extrasystoles in patients with mitral stenosis presage the appearance of auricular fibrillation. Multifocal extrasystoles are usually accompanied by severe myocardial disease. At times extrasystoles are closely linked with progressive disease of the coronary arteries. Because such extrasystoles may be followed by sudden death, presumably due to ventricular fibrillation, the prophylactic use of quinidine sulphate is indicated. The majority of patients with either ventricular or auricular extrasystoles occurring during rapid heart rates had definite, and usually advanced, myocardial disease. The occurrence of extrasystoles with active Graves' disease suggests an associated cardiac lesion. Extrasystoles are usually without clinical significance when not associated with one of the above conditions.

The Treatment of Coronary Artery Disease by Intravenous Injections of Hypertonic Saline Solution. S. C. FEINBERG. Am. J. Med. Sci. 191: 410, March 1936.

Six patients suffering with advanced coronary artery disease were treated by the intravenous administration of hypertonic saline solution. They had previously been treated for periods of six months or more by the usual measures without relief.

Under saline therapy after six months they have responded to the treatment and maintained their improvement, although previously none had been able to walk more than a block without anginal symptoms, and some had had precordial attacks even at rest. This treatment is based on the work of Sibert in thromboangiitis obliterans. It is the belief of the author that the intravenous injections result in an increased collateral circulation in the heart and in this way yield the satisfactory results reported.

Toe Lesions Following Tobacco Injections in Rats. M. FRIEDLANDER, S. SILBERT AND N. LASKY. Proc. Soc. Exper. Biol. & Med. 34: 156, March 1936.

A series of 48 male and 12 female albino rats were treated with daily intraperitoneal injections of tobacco extract from which most of the nicotine had been removed. In 33 of the 48 male rats gangrene of the toes developed within five to twelve weeks. None of the 12 female rats, injected daily for five to eighteen weeks, developed this lesion. In 10 control male animals, living under identical conditions, no gangrene developed. One male animal subjected to daily inhalations of tobacco smoke for a period of five months developed gangrene of the toes. One animal treated with daily intraperitoneal injections of alkaloid nicotine tartrate also developed a characteristic lesion. Microscopic studies are being made of the blood vessels of the extremities.

Retro-Esophageal Goiter. J. H. Garlock. Surg. Gynec. & Obst. 62: 616, March 1936.

Retro-esophageal goiter is a definite clinical entity which may be diagnosed before operation. Characteristic symptoms are a sense of constriction about the neck, attacks of choking, especially when turning the head away from the side of entrance of the goiter in the retro-esophageal space, spells of coughing, dysphagia, and hoarseness of variable intensity. The probable diagnosis of retro-esophageal goiter should be kept in mind if it is possible to determine anterior displacement of the trachea against the upper edge of the manubrium. Retro-esophageal extension of a goiter may be graphically depicted by lateral roentgenograms of the neck showing anterior displacement of the trachea, and also after the ingestion of a barium mixture, to outline the position and shape of the esophagus. The operative technique is discussed.

A Diabetic Primer for Children. ELLA M. COLEMAN AND ALFRED E. FISCHER, M.D. Pp. 42, 4 illustrations. New York: Mount Sinai Hospital, 1935. (Review from Am. J. Dis. Child. 51: 1493, June 1936).

"The authors have written a pamphlet in the second person which is intended for the child in the grade schools who cannot comprehend the usual primers on this subject. They have succeeded admirably in simplifying terminology.

The new classifications of fruits and vegetables recently accepted by the American Dietetic Association have been included. In the sample diets the fats and proteins remain about the same in amount, while the amount of carbohydrates is varied according to age. Each diet therefore has a considerable variation in the ketogenic-antiketogenic ration. There is a good list of substitute foods. The food recipes are devised to appeal especially to the child.

The method of administration of insulin is explained in detail. The reaction to insulin is well described, so that the child should not be unduly alarmed but rather well educated and prepared to cope with it. In the description of approaching coma the authors fail to indicate the necessity for tests for the ketone bodies in the presence of illness or persistent increasing glycosuria."

NEWS AND NOTES

GENERAL MEDICINE

General bedside therapy.   DR. D. POLL.
Clinical bacteriology and immunology.   DR. G. SHWARTZMAN.
Practical course in clinical bacteriology.   MISS C. HERSCHBERGER.

DISEASES OF CHILDREN

Clinical pediatrics: A comprehensive course in diseases of children.   Instructors:
   DRS. B. SCHICK, H. SCHWARZ, M. H. BASS, B. S. DENZER, J. L. KOHN,
   S. KARELITZ, A. E. FISCHER and G. J. GINANDES.
Nutrition of infants and older children.   Disorders of nutrition.   DR. B. SCHICK.
Heart disease in children.   DR. I. R. ROTH.
Conduct disorders of children.   DR. I. S. WILE.
Asthma in children.   DR. M. M. PESHKIN.
Diabetes mellitus in children.   DR. A. E. FISCHER.

GYNECOLOGY

Gynecological diagnosis, treatment and pathology. DRS. S. H. GEIST, M.D. MAYER,
   U. J. SALMON and J. A. GAINES.
Clinical course in gynecology together with a survey of gynecological pathology.
   DRS. I. C. RUBIN, M. A. GOLDBERGER, P. BERNSTEIN, S. WIMPFHEIMER and
   E. KLEMPNER.

OPHTHALMOLOGY

Ophthalmoscopy.   DR. K. SCHLIVEK.
Ophthalmic surgery.   DR. I. GOLDSTEIN.
Ophthalmic neurology.   DR. R. K. LAMBERT.
External diseases of the eye and technic of examination.   DR. H. MINSKY.
Refraction and muscles.   DR. J. LAVAL.
Pathology of the eye in general disease.   DR. D. WEXLER.
Embryology of the eye.   DR. A. L. KORNZWEIG.

PHYSICAL THERAPY

Physical therapy for the general practitioner.   DRS. W. BIERMAN, C. L. LEVENSON
   and S. LICHT.

Pathological chemistry. Dr. H. H. Sobotka.

Routine chemical methods as used at The Mount Sinai Hospital. Miss M. Reiner.

Courses Offered from January 17th–March 12th, 1938

GENERAL MEDICINE

Diseases of metabolism. Drs. G. Baehr, H. Lande, H. Pollack, L. J. Soffer and Miss A. Wood.

A course in diagnosis and therapy. Drs. B. S. Oppenheimer, E. Moschcowitz, R. Ottenberg, D. Beck and Staff of Second Medical Service.

Diseases of the kidneys and arteries. Dr. E. Moschcowitz.

Diseases of the liver and biliary passages. Drs. R. Colp, P. Klemperer, S. S. Lichtman, R. Ottenberg and H. Sobotka.

Clinical manifestations of coronary artery disease. Drs. E. P. Boas and H. Levy.

Practical pharmacology. Dr. H. T. Hyman.

Practical hematology. Dr. N. Rosenthal.

Clinical electrocardiography. Drs. A. M. Master, H. L. Jaffe and S. Dack.

Diseases of the heart: Clinical features interpreted through roentgenologic, anatomic and histologic findings. Drs. A. M. Master, C. K. Friedberg, P. Klemperer and Morbid Anatomy Staff.

Clinical features of irregular heart action. Dr. I. R. Roth.

Allergy: Its relation to internal medicine. Dr. J. Harkavy.

Diseases of the chest. Members of the Chest Group: Drs. H. Neuhof, A. S. W. Touroff, C. B. Rabin, H. Hennell, and I. S. Schapiro.

Practical course in peripheral vascular disorders. Dr. S. Silbert.

Clinical cardiology with particular reference to endocarditis. Dr. S. H. Averbuck.

General and special pathology. Drs. P. Klemperer and S. Otani.

Surgical pathology. Drs. P. Klemperer and S. Otani.

Advanced Course in Cardiology

Four weeks' intensive course. Instructors and hours to be announced later.

ENDOCRINOLOGY

Gynecological endocrinology. Laboratory course in bio-assay of female and male sex hormones. Drs. R. T. Frank, M. A. Goldberger, U. J. Salmon, G. Felshin and E. Klempner.

GASTROENTEROLOGY

Diagnosis and treatment of diseases affecting the gastrointestinal tract. Drs. B. B. Crohn, A. Winkelstein, E. Granet, B. Kornblith and H. Yarnis.

Four weeks' intensive course. Gastroenterology: Its relation to internal medicine and abdominal surgery. Instructors: Drs. G. Baehr, R. Colp, B. B. Crohn, H. Doubilet, J. H. Garlock, S. J. Goldfarb, E. Granet, F. Hollander, P. Klemperer, B. Kornblith, B. S. Oppenheimer, R. Ottenberg and A. Winkelstein. (Time to be announced later.)

PROCTOLOGY

Intensive course in office proctology.   DRS. R. COLP, S. D. MANHEIM, A. GOLD-
SCHMIDT and L. J. DRUCKERMAN.

NEUROLOGY AND PSYCHIATRY

Applied neuroanatomy and neuropathology.   DR. J. H. GLOBUS.
Psychoanalysis in medicine.   DRS. C. P. OBERNDORF and A. SLUTSKY.
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CONTENTS

Introductory Note

THIS ISSUE of the Journal of The Mount Sinai Hospital is dedicated to

DR. RICHARD LEWISOHN

on the occasion of his completion of thirty years of active duty on the surgical division of the hospital.

His colleagues and friends have joined to express through this medium their best wishes and their appreciation of his services to surgery and medical science.

Henry Goldstein

SOME FUNDAMENTAL PRINCIPLES OF THE ETIOLOGY OF PEPTIC ULCER; THEIR APPLICATION IN TREATMENT*

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Some of the methods employed in the treatment of peptic ulcer are surprisingly efficient in controlling the symptoms of this disease. The word "surprisingly" is used advisedly because many methods of treatment utilized with at least temporary success are not based on sound physiologic reasoning. In many instances, of course, the alleged cure may represent merely the periodic progression into a stage of rest which might have occurred even though no treatment whatsoever had been advised. Certain surgical operations, such as partial gastric resection and gastro-enterostomy, are based on a more logical process of reasoning. In these therapeutic procedures an effort is made to change gastric physiology permanently. Partial gastric resection removes much of the diseased tissue; adequate emptying of the stomach is facilitated and reduction of acidity is accomplished. In the case of gastro-enterostomy the highly important mucus-producing portion of the stomach is retained, emptying is assured, provided the stomal opening is sufficiently large and properly placed, and a definite reduction of acidity usually results.

Medical regimens often fail to cure peptic ulcer because they make no provision for the prevention of recurrence. After the symptoms of the individual exacerbation have been controlled, the patient is given general, and usually all too vague, instructions for the immediate future and then is left to forage for himself until such time as recurring difficulties force him to consult the physician again. Another cause for failure of medical treatment is the improper selection of cases. In many cases of peptic ulcer there is associated disease elsewhere, or the lesion is in such a condition histopathologically that there is little hope for permanent relief of symptoms from any but surgical procedures. Failure of non-surgical treatment is not infrequently due to the fallacious presumption that cessation of symptoms indicates a healed ulcer with consequent relaxation in methods of treatment. An unhealed ulcer does not always produce symptoms. At The Mayo Clinic we have often observed an open, active peptic ulcer at operation without any symptoms to indicate the presence of such a lesion. In commenting on the end results of the medical treatment of peptic ulcer Moynihan said: "Relief of an attack in a case of

chronic duodenal ulcer is easy; a cure of the condition by medical means is, I believe, almost impossible." Although it is true that some ulcers are intractable to medical or even to radical surgical treatment, one is not justified in ignoring the fact that in many cases patients remain well after medical regimens. Admittedly, certain ulcers heal spontaneously without definite treatment. On the other hand, others which respond to treatment only after the most carefully planned regimens can be demonstrated to have healed soundly when inspected at operation performed subsequently for some other disease.

<div align="center">ETIOLOGY</div>

In order to proceed reasonably with the problems of therapy of peptic ulcer, one must have some rational ideas regarding its causes. Although there are many interrelated factors which are important in the causation of this disease, these ultimately resolve themselves into the two which follow: (1) the inherent ulcerating potentiality of acid-pepsin, and (2) the defenses which are available to the tissues by which they protect themselves against the eroding action of the gastric chyme. It would seem that the alternating activity and quiescence which are so characteristic of such lesions would be evidence of contrary forces, one of assault and another of defense, and that the outcome would depend on which factor was dominant at any particular stage of the life cycle of this disease.

The Assault of Acid-pepsin on Gastroduodenal Tissues. Physiologists have demonstrated experimentally with animals that the component fraction of gastric juice which can produce erosion resides in the acid-pepsin factor. The eroding tendency fluctuates, not with variations in peptic concentration, but with the concentration of hydrochloric acid. Tissues laved in pure undiluted gastric juice are very likely to undergo erosion. Mucous membranes which in their normal physiologic existence are regularly exposed to the acid chyme possess definitely more resistance to its eroding action than do those which are not normally bathed in gastric juice. Gastric mucosa is more resistant to the processes of erosion than are other tissues. Although the duodenum has a remarkable reserve function in its capacity to neutralize and to buffer acid, it has been shown by Mann and Bollman (3), Baker (1), Florey and Harding (2), that it will break down under the necessity of neutralizing *without interruption* the acid chyme. Ordinarily, in the daily physiologic fluctuation of gastric acidity there are alternate periods of rapidity and retardation in the secretory rate, thus giving the cells bathed in this chemical atmosphere "breathing spells" during which their forces of defense can be adequately reestablished. Physiologists have shown that the continuous feeding of hydrochloric acid is likely to cause the eventual breakdown of cells called on to resist the digestive action of the gastric chyme. The experimental observations just described are not without pertinent corollaries in clinical

experiences with certain patients harboring peptic ulcer, particularly those found to have duodenal or jejunal ulcers. The gastric secretory rates of such patients are usually accentuated, particularly during or preceding periods when there is definite activity of the ulcer. Following subcutaneous ingestion of stimulating substances, such as histamine, patients who have peptic ulcer frequently continue to secrete a highly concentrated acid for considerable periods after a drop in acidity would ordinarily have been expected. If such cellular behavior actually obtains in response to other stimuli, it would seem to be obvious that the gastroduodenal defense mechanisms of patients who have peptic ulcer might be forced to exert themselves accordingly. It seems logical that the activity of the mechanisms of defense would have to fluctuate in proportion to changes in the potency of the mechanisms of aggression. The importance of neurogenic factors in relationship to the etiology and recurrence of peptic ulcer has often been pointed out. Certain individuals have an increased tendency to the formation and reformation of peptic ulcers. Efforts to categorize these factors into definite groups by various physical measurements have not been successful because the distinguishing features seem more psychophysiologic than physical and anatomic. A striking uniformity of temperament is noted in a certain group of patients who have peptic ulcer. They are persistent in their activities and possess unusual physical and mental drive. They seldom relax, and they are alert, attentive, and keen. They often are unusually introspective, suspicious, sensitive, and given to periods of worry and depression. The periodicity of symptoms in cases of ulcer frequently is determined by variations in the psychophysiologic influences incident to the daily experiences of the patient. During periods of unusual and unrelieved worry and tension, symptoms are likely to originate or to be reestablished. Marked elevation and unusually prolonged persistence of accentuation of the gastric secretory rates are often noted during periods of excitement and tension, and it may be that one of the mechanisms of the formation of ulcer in this group of patients is related directly to gastric chemical conditions which are thus affected by disturbances in the nervous system.

Defenses of Tissues Against Erosion by the Acid Chyme. Nature has provided that the factors tending to erosion, which are inherent in acid-pepsin, are ordinarily insufficient to produce ulceration in tissues which maintain their normal mechanisms of defense. The neutralizing effect of alkaline blood in mucosal capillaries, the protective action of gastric mucus, the presence of alleged antipepsin in the gastric mucosa have been considered as a partial explanation of the obvious mechanisms of defense in gastric tissues. An important factor responsible for the increased resistance of the duodenal cells to ulceration is inherent in the glands of Brunner, which under the necessity of neutralizing acid chyme suffuse the duodenal membranes with a protective coating of an alkaline mucoid

secretion. The disarming importance of the secretions which are poured into the duodenum by organs which are extrinsic to the gastro-intestinal tract must not be underestimated. Bile and pancreatic juice have been shown to be of definite importance in protecting gastroduodenal tissues against erosion by acid chyme. Furthermore, it may be one of the functions of certain hormones elaborated by the wall of the upper portion of the intestinal tract, among which is enterogastrone, to retard the gastric secretory rate in emergencies. Furthermore, in considering defenses of tissues, one is likely to forget a factor of crucial importance, namely, the inherent resistance of the cell itself. A properly nourished cell possesses a remarkable integrity and hardiness. The breakdown of tissues probably results not from one but from various causes. There may have been localized anomalous tissue or a vascular defect in the gastroduodenal wall; resistance of the tissues may have been diminished by debilitating systemic disturbances.

Unquestionably one of the important causes of the cellular dissolution which results in peptic ulcer lies in the exhaustion of the intrinsic and extrinsic cellular defense. The mucoid covering of the epithelium, the natural buffers and alkalies and the individual cellular resistance, all combined fail to resist the onslaught of the overwhelming forces of persistent hyperacidity. The forces of erosion, through the utilization of an inherent chemical factor alone, can in experimental animals break down normally resisting tissues and cause ulceration. There is no reason to assume that human tissues behave differently.

If normal tissues can disintegrate under the prolonged bombarding influence of highly aggressive acid chyme, it is not difficult to assume increased liability to ulceration in tissues deficient in capabilities of defense.

Various influences may produce injury to the mucous membrane or to the gastroduodenal wall, and these may involve the mucosa or originate with disturbances in the submucosa. Shallow erosions may be associated with systemic diseases, such as purpura or certain infectious diseases. Similar disturbances in tissue have been demonstrated by Rosenow (5), who suggested that septic emboli, the result of focal infections, may settle as small nests in the depths of gastroduodenal tissues, and, destroying resistance locally, tend toward the formation of ulceration. The chronic inflammatory changes in the pyloric antrum, so frequently seen in association with peptic ulcer, have been stressed as a precursor rather than a sequel of formation of ulcer. It has been pointed out that they may result from a variety of causes; irritating substances, which have been ingested, and roughage may cause mucosal injury. Gastric ulcers arising in association with foreign bodies, as well as ulcers occurring at the point of maximal mucosal irritation in conjunction with diaphragmatic hernia, would be further illustrations of insults to local tissue, which have been shown to be of some importance in causing ulcer or in keeping an ulcer from healing.

In all probability chronic ulcer will seldom develop from these factors alone. Most of these lesions represent only one of the stages of chronic ulcer. For the accomplishment of chronic peptic ulceration, assistance will be necessary from other factors which keep the original lesions from healing.

There is much to suggest that peptic ulceration should not be considered a definite specific single disease entity.

It would seem to me that it is a single disease entity only so far as it represents a form of dissolution of tissues that occurs in the presence and in consequence of the eroding action of the acid gastric chyme. It is the local manifestation of a disturbance in the gastroduodenal tissues which in turn may be initiated by various systemic causes. It is no longer possible to dismiss the discussion of the genesis of ulcer with the complacent assumption that the etiology of this disease is unknown, although it must be admitted that no single, fixed, immutable, causative agent has been discovered which is invariably responsible for the formation of ulcer; in all probability, no such single causative factor exists.

In my opinion the stubborn insistence that it is necessary to demonstrate a single causative factor which is invariably responsible for peptic ulcer has hindered rather than helped progressive thinking regarding etiology and therapeusis of the diseases included in the term "peptic ulcer."

The multiplicity of the ways in which peptic ulcer can be produced in experimental animals suggests that peptic ulcer in the human being may also be produced in diverse ways. Instead of attempting to assemble the various methods of the genesis of ulcer into a single composite etiologic picture, which is hopelessly indistinct, might it not seem more logical to dismember the hypothesis and reconstruct these disjoined facts into several pictures which are reasonably distinct and simple?

There is no fixed constant in the production of peptic ulcer. The acid chyme is probably the only common denominator invariably concerned in ulcer production. It is the "sine qua non" of peptic lesions. One must not harbor the idea that even this factor is a fixed one. Admittedly, the more concentrated the acid, the greater its ulcer-producing tendency; there is, however, no level of concentration above which there is ulcer and below which there is safety. This hypothetical divide is again a fluctuant one depending on several factors. Alternating accentuation and retardation of secretory rates are important. There is an element of safety in this. As a rule, even healthy tissue cannot withstand the eroding onslaught of persistently elevated secretory activity.

Chemical Peptic Ulcer. This hypothesis can be illustrated by the review of the case of a man, aged forty-six years, who had experienced indigestion typically characteristic of ulcer for twenty-six years. Roentgenologic studies revealed evidence of a duodenal ulcer. Test meals

showed hyperacidity. Histamine test showed concentration of 148 units of free hydrochloric acid as long as eighty minutes after the test was started. The secretion of pepsin ranged between 1520 and 2840 units. Recurrences were frequent and this is not surprising if the chief and parietal cells responded to other stimulation as they did in this instance to histamine. This case probably illustrates the most frequent type of peptic lesion which might be called chemical peptic ulcer. The situation of the ulcer would be determined by a physical factor, that is the point of maximal irritability which is variable in different individuals, usually duodenal in location, at the point whereon the pyloric nozzle impinges the irritating chyme.

Neurogenic Peptic Ulcer. This probably represents a subdivision of the type of ulcer just considered, the chemical factor being unusually aggressive and whipped into action by an unusually disturbable nervous system. At the clinic we have often noted a marked tendency for prolonged elevation of secretory rates in tense, nervous, unrelaxing individuals who have peptic ulcer. Perplexing, unrelieved difficulties usually act as so many histamine cellular stimulants (that is, causing elevated acids) which promptly precipitate these patients into recurring episodes of ulcer activity. As an illustration of this group of peptic ulcerations one may consider the case of a man, aged thirty-one years, who for some time had experienced intervals of indigestion caused by a duodenal ulcer. Studies of gastric contents showed hyperacidity. His wife became ill, and he promptly had an episode of distress. Later, his son had a serious illness and again his ulcer became active. Following the death of his son, he had more indigestion. With each seriously disturbing experience there had been a period during which his ulcer had caused trouble.

Untamed chemical and mechanical factors may not be the only ones which accomplish reactivation of ulcer in patients included in the two groups just discussed. There may be anomalous disturbances of tissues or other conditions may supervene which temporarily and periodically diminish resistance of tissues and thus facilitate ulceration by a chyme which without this contingency would have remained harmless.

Unsurmountable difficulties develop if one insists on explaining the genesis of all peptic ulcers on the basis of disturbances in the cellular behavior of the chief and parietal cells alone. There are other groups of peptic ulcers in which the disturbance permitting ulceration to occur originates in the gastroduodenal tissues themselves.

Infectious Peptic Ulcer. I am at the present time reviewing a large number of histories of patients with peptic ulcer to ascertain the various etiologic factors important in the formation of the lesions. Among these there are many cases in which careful study of the chemical constituents of the gastric chyme fails to show any unusual responses. The acidity is not abnormally high and peptic activity is not unusual. The reaction

of the chief and parietal cells to the stimulating effect of histamine shows
no tendency toward persistent accentuation of secretory rates. There is
no hint throughout the entire life cycles of these ulcers to suggest that re-
currences are brought about by psychic trauma, nor are the patients of
the nervous, high-strung, intensive type. The history may include evi-
dence suggesting the relationship of intercurrent infections and recurring
symptoms. Hemorrhages or acute exacerbations of distress caused by
this ulcer may have coincided in time to acute tonsillitis or infection of the
upper part of the respiratory tract. An inflamed appendix or gall-bladder
may be the focus from which infection spreads to the walls of the duo-
denum or stomach, which would appear able to diminish the threshold of
resistance so that even normal forces of assault inherent in the erosive
faction of the gastric chyme could cause dissolution of tissue and even-
tually cause chronic ulceration. Impressive in illustrating this type of
ulcer is the case of a little girl, aged five years. In this case the first evi-
dence of any difficulty was an attack of tonsillitis. She promptly began
to complain of pain in her stomach and shortly after this she vomited
copious amounts of blood. Roentgenograms showed a duodenal deform-
ity. The tonsils were removed. Cultures from these injected into ex-
perimental animals produced hemorrhages and ulceration throughout the
upper part of the gastro-intestinal tract. A bland diet was advised for
several months. There has been no evidence of recurring ulceration.
There are mixed types in which at one time chemical factors are impressive
and at other times the factor influencing recurrences seems to be specifi-
cally related to infection.

Traumatic Peptic Ulcer. A review of various types of peptic ulceration
must not fail to include ulcers, gastric in situation, which so often are found
associated with foreign bodies of the stomach. Occasionally, such ulcers
are found at the point where a herniation of the organ through the dia-
phragm has occurred. These lesions usually are found in the region of
maximal traumatic irritation. Actual ulceration is in all probability still
caused by the acid-pepsin constituent of the gastric chyme but that this
in itself is inadequate to maintain active ulceration in these particular
cases is evidenced by the fact that when the irritating factor ceases to
exist the ulcer promptly goes on to complete and permanent healing.
The patients harboring this type of ulcer are not of the nervous, intensive
type who are so likely to develop chronic duodenal ulcer. The tendency
to recurrence is not marked. Secretory behavior of the chief and parietal
cells is not unusual. This type of ulceration is illustrated in the case of a
woman, aged forty-nine years, who complained that for twelve years she
had experienced almost daily digestive disturbances. Large meals caused
discomfort in the left upper abdominal quadrant. Vomiting of copious
amounts of blood had occurred on several occasions. Roentgenologic
investigation showed an esophageal diaphragmatic hernia and a gastric

ulcer. At operation the ulcer was found in the region where the rupture had occurred through the diaphragm. The hernia was reduced. Despite the fact that no local treatment was directed to the ulcer, subsequent ro-entgenologic investigation showed a healed lesion and there has been no history of recurring indigestion.

Peptic Ulcer Related to Nutritional Disturbances. In the peptic ulcers related to infection and to mechanical irritations of gastroduodenal mu-cosa the individual cells are likely to maintain their inherent natural resistance, being affected only secondarily by infection of contiguous tissue or by actual physical injury. Evidence is accumulating to suggest that in certain instances capillaries and cellular integrity may be decidedly abnormal because of nutritional disturbances related in some instances to demonstrable vitamin deficiencies. It is not difficult to assume that with a definite diminution in cellular hardiness ulceration could easily be accomplished in the presence of acid and pepsin of normal erosive poten-tialities. Of some interest in this regard is the case of a clergyman, aged forty-eight years, who lived in a mission house in China. It became neces-sary for him to make a tour of the inland churches. Several weeks after beginning his journey, during which he ate native food, indigestion devel-oped. Assuming that this was due to dietetic causes, he had curtailed the intake of food until he was living on a very inadequate diet consisting of a few of the native vegetables. Two weeks after the onset of the indiges-tion he had a gross gastro-intestinal hemorrhage. When he came to the clinic he was found to have a duodenal ulcer. The gastric acidity was not unusual. Histamine studies revealed secretory rates which were not ab-normal. Capillary resistance to the pressure cuff was definitely dimin-ished. There was marked deficiency of vitamin C in the plasma and urine. Adequate feeding and supplementary administration of cevitamic acid was followed by prompt clinical improvement. Within a week the plasma and urine contained a normal amount of vitamin C. Capillary fragility returned to normal as soon as the vitamin C in the plasma was restored to normal. The patient has remained well since he has been on more adequate diets. The amount of vitamin C in the plasma is in all probability not the only cause of the diminution of the resistance of the capillaries and tissues in such instances. Experimental work is now being done to ascertain other related vitamin deficiencies. It would seem that too strict dietetic restrictions may hinder rather than stimulate healing of peptic ulcers in certain instances.

This paper is not intended to be a disquisition on the multiformity of peptic ulcer. What I have said regarding this subject is elementary. Neither time nor space permits more than passing mention of other forms of gastro-intestinal peptic ulcerous disease, such as the peptic lesions so often associated with renal, hepatic and prostatic disease, ulcers following burns, ulcers associated with intracranial lesions, and ulcers occurring

about Meckel's diverticuli, which contain heterotopic gastric tissue. It is my intention to devote more attention to this particular phase of the subject in a subsequent publication. Suffice it to say here that it would seem that even the most skeptical would agree that no single immutable formula for all peptic ulcers is conceivable. Consider the difficulty of fitting into one etiologic pattern the gastric ulcer associated with foreign bodies of the stomach and the oft recurring chronic duodenal ulcer which is associated with capricious secretory activity and which gets out of control on the slightest provocation. Similar difficulties would also be encountered in attempting to colligate etiologic theories regarding the peptic ulcer precipitated into activity by seriously disturbing worries and cares with one complicated by hemorrhage and occurring in a child following tonsillar infection. It is not so important whether these are considered different types of peptic ulcer or merely varying etiologic factors in the same disease. What is important is the necessity of appreciating that the behavior of these ulcers, the prognosis, the tendency to recurrence, the ease of reactivation, and, particularly, the treatment of such lesions demand special consideration in individual cases.

TREATMENT

The life cycle of an ulcer includes little that is fixed and static. Through it move several forces in ever changing potency; chemical forces of aggression are opposed by forces of tissue defense; now local and now systemic disturbances add potency to one or the other of these factors and influence the balance which results in healing, persistence, or progression of the ulcerating process. Obviously, the contending play of these forces demands special and individual consideration in the therapeutics of this disease. Since this is true, no prearranged, ready-made treatment is possible. Furthermore, since it is impossible for patients who have peptic ulcer to live under the constant, watchful supervision and guidance of their physicians, it is obvious that these patients must understand something about the problems incident to their disease and must be trained to contend with them as they may arise. For this reason it has been our custom at the clinic for some time to hospitalize all these patients for a brief period of education, as well as for instituting a medicinal and dietetic regimen, so that the varying factors which seem important in the causation and course of this disease can be detected and treatment advised accordingly. This educational program applies to surgical as well as to non-surgical cases. With this instruction, in which incidentally these patients are remarkably interested, a new understanding and consequently a spirit of cooperation develop, wherein lies much hope for a greater eventual success in the handling of this disease.

Control of Symptoms. The first essential in the treatment of peptic ulcer is to recognize if any complications such as perforation, hemorrhage, or

obstruction have occurred. It is, of course, essential to establish proper methods of treatment to care for such complications if they be present. Unless some serious complicating factor supervenes, it is as a rule not difficult to accomplish the control of symptoms caused by peptic ulcer.

The symptoms are controlled with much greater facility if these patients are kept in bed. It is important that they be thoroughly relaxed. This can usually be accomplished by adequate amounts of bromide or barbiturates. The diet should consist mainly of milk, given at frequent intervals, and the judicious use of alkalies and atropine hastens return to a comfortable status. There is much controversy regarding the use of various substances, such as larostidin, synodal and vaccines, to accomplish the control of symptoms. In an effort to hasten initiation of healing, others advise discontinuing the ingestion of all food by mouth and giving nutritional enemas during this period. Still others advise the use of intragastric, intraduodenal, or jejunal feedings accomplished by means of small jejunal tubes. If patients do not respond to the simpler methods of treatment, any of these methods of therapy can be tried, but we seldom use them at the clinic.

Planning a Regimen to Promote Adequate Healing. After the activity of the ulcer has abated and the patient has become symptom-free, it becomes necessary to formulate a plan which will most efficiently accomplish healing of the lesion. It should not be assumed that quiescence of symptoms indicates a healed or even a healing ulcer; this is a common delusion and one which only too often results in therapeutic failures. With the cessation of symptoms it becomes possible to make a more thorough physical examination and to evaluate the history more leisurely and thoughtfully. The behavior of rates of gastric secretion should be studied and roentgenologic investigation must not be neglected.

Under the discussion of the etiology of peptic ulcer the causes interacting in its production were considered under two heads: first, the assault of acid-pepsin on gastroduodenal tissues, and, second, the defenses of tissues against erosion by the acid chyme. The physician who wishes to treat ulcer successfully will devote attention not only to the control of the acid factor, but he will also direct his efforts toward restoring normal resistance of tissues. He will furthermore ascertain by careful study the type of ulcer he has accepted the responsibility of treating. Aided by this information he will then be able to direct treatment more intelligently and consequently more effectively.

Diet. The first step in the control of acidity consists in the selection of a correct diet. This should be non-irritating and should contain the various food elements in proper balance; it must include adequate amounts of vitamins and minerals. The diet should not unduly provoke the secretion of acid and it should be able to neutralize acids by combining with them. In some instances gastric acidity can be controlled by means of frequent feedings alone.

At the clinic we practically never find it necessary to restrict the intake of food as drastically or for as long as is suggested with most other methods of treatment. The amount of food taken is increased rapidly, so that within eight to ten days the patients are usually taking an adequate, though bland, type of diet. This diet is then continued for a period of six months to a year, during which time supplementary feedings between meals and before retiring are advised. It is felt that even after active treatment of the individual exacerbation is completed, the patient should continue to avoid eating stimulating foods or taking drinks that would cause elevation of the gastric acidity.

Alkalies. The adequate reduction of gastric acidity usually requires the use of alkalies. It has been the custom at the clinic to administer 200 to 300 grains (13.0 to 20.0 gm.) of alkali daily, in divided doses. If administration of this amount of alkali does not control acidity, three to four times the amount may also fail to lower it. The indiscriminate dumping of increasing amounts of alkali into the stomach to force neutralization of acids seems an unphysiologic and, at times, a dangerous procedure.

In certain cases the use of alkalies and a bland diet promptly reduces the acids to entirely satisfactory levels, and throughout the course of treatment no unfavorable responses are noted. There are other cases, however, in which it can be shown that the gastric chyme maintains tremendously high levels of acid concentration, and the values for pepsin in such instances are often grossly accentuated. It is noticeable in some of these instances that if the acidity has been reduced by means of intensive treatment it rebounds to uncomfortable levels at the slightest provocation. The condition in such cases can sometimes be controlled by continuing a stricter diet for a longer time. The administration of alkalies should be continued at frequent intervals, and, sometimes, a change from one to another form of alkali will accomplish reduction of acidity. Large doses of atropine may also help. The repeated use of olive oil throughout the day, and particularly in rather large doses immediately before retiring, may be of value. In such instances it frequently is obligatory to prevent the use of tobacco. In these cases it usually is essential to insist on intensive regimens and continuation of all measures instituted to control acids for a long time, even after symptoms have been relieved.

It is essential through this period of treatment to encourage these patients and it is absolutely necessary to keep them properly relaxed. Details of instruction and discussion regarding neurogenic factors will be considered under the prevention of recurrences.

Any plan of treatment for peptic ulcer should include some provision for the search and eradication of such causes as seem capable of producing injury to gastroduodenal tissues. The proper recognition of the type of ulcer under consideration here becomes of obvious value. Special therapeutic measures must then be applied to counteract the particular etiologic

factor predominantly important in specific instances. Apparently, such innocuous disturbances as common colds or mild infections of the upper part of the respiratory tract often precipitate recurrences of symptoms, and hygienic measures to avoid these, as far as possible, are part of the program of treatment. The eradication of foci of infection in special cases may aid materially in controlling the activity and preventing the recurrence of such peptic ulcers. Apart from dealing with infections of the teeth, tonsils, accessory sinuses, and the prostate gland, surgical treatment has at times to be directed to the gall-bladder and appendix if clinical evidence has pointed to involvement of these organs. Finally, debilitating conditions which tend to diminish the defensive power of the tissues require specific attention in addition to measures directed toward the healing of ulcer. More frequently, perhaps, than one might wish to admit, the lack of necessary accessory food factors, arising from prolonged and enthusiastic adherence to restricted diet, may so undermine the patient's resistance as to militate against, rather than assist in, the healing of an ulcer. It is particularly important to include enough vitamins in the diet. Recently, we have had opportunity to study the results obtained in cases of ulcer after feeding large amounts of vitamins, particularly vitamin C. It seems to us that these patients have made an unusually satisfactory response to treatment. There are other instances in which special local attention to traumatizing influences will promptly result in the cure of such lesions. One need only consider, as examples, gastric ulcer associated with such foreign bodies in the stomach as hairballs or bezoars, and similar lesions which develop in cases of diaphragmatic hernia at the point at which herniation through the diaphragm takes place. In these cases prompt cure of the ulcer results when the cause of irritation is removed or corrected.

PREVENTION OF RECURRENCES

The first prerequisite to the prevention of recurrence is an understanding on the part of the physician and patient that the individual breakdown of tissues is a mere link in the chain of the life cycle of ulcer. The physician must not be satisfied when he has accomplished cessation of symptoms; he should insist on continuation of intensive methods of treatment until there is evidence that adequate healing of the ulcer has taken place. It is absolutely essential that the patient should understand that his disease remains a perennial problem. I attempt to explain to such patients that the ulcer can be likened to a brook in a meadow and that periods of activity of the ulcer correspond to periods of flood when the entire meadow is inundated. After the waters recede into their normal channels everything looks serene and peaceful, but the brook, like the ulcer, is still there. By proper precautionary measures floods may be avoided or their destructive force mitigated. Such a patient is made to understand that at certain

times the tendency to recurrence is increased and that at these times addi-
tional precautions are necessary.

While the patient is in the hospital we attempt to acquaint him as
thoroughly as possible with the nature of his disease. The patients and
resident physicians meet several times in the period of hospitalization for
group discussion. An effort is made by means of drawings, pictures,
graphs, and photographs to teach the patients elementary, anatomic
and physiologic facts and something about the cause of their disease.
Factors which tend to produce recurrences are considered. In addition,
the factors which decrease the resistance of the tissues, such as infections
and vitamin deficiencies, are mentioned and patients are instructed in
methods of keeping the resistance of tissue at normal levels. Nervous
tension, fatigue, worry, irregular living and dietary habits, abuse of
alcohol and tobacco, the use of condiments and rough, irritating foods
are all considered, and it is pointed out how gastric chemistry or
mechanics may be influenced by various abuses.

At an individual conference with his physician each patient talks over
his own problem and is helped to outline a method of living which will aid
in the development of greater equanimity

Certain patients deny the relationship of periods of worry and strife to
their symptoms and yet closer questioning and observation leaves little
doubt as to the intimate relationship between the two. There are some
patients whose external appearance of composure and tranquillity hides
a veritable turmoil of emotions which remain buried and unsuspected
until careful study and kindly investigation stimulate the understanding
and confidence which bring them to light. When the importance of
these nervous factors is discussed with the patient, he frequently begins
a search through his past experiences and often he is able to satisfy him-
self as to the interrelation of worry and his symptoms. With the dawn
of this understanding comes confidence and then cooperation. With
this the battle is half won. It then becomes less difficult to convince the
patient that it is necessary to avoid unusual mental fatigue or unnecessary
responsibility even when he is feeling well. Sometimes, it is possible
to change the patient's mental reactions to the usual disquieting influences
incident to daily life. A very serious obstacle which blocks the way to-
ward permanent recovery will have been removed if the patient can be
taught to accept these experiences less impetuously, to do things more
slowly and less intensely. and to develop a spirit of equanimity toward
incidents tending to perturb and worry him.

At times, it is possible for the patient to arrange his work so that he can
devote some time each day to play or to the pursuit of some hobby. He
should be encouraged to take more vacations and, whenever possible, he
should arrange to be away from work for part of the day, several times
each week. I usually encourage the patient to lie down and rest for a

time after the noonday meal. He should also utilize the occasion of the supplementary feeding he takes between meals as a brief respite from worry and work. He should be advised to get nine or ten hours of sleep at night, and if this is not possible without sedatives, I frequently advise small amounts of bromides or barbiturates.

The dietitian in charge also holds individual and group conferences when she helps the patient to outline a sane, liberal, dietetic regimen, without unnecessary restrictions, which he can follow permanently. The patients, almost without exception, leave the hospital with new hope and with assurance that they can manage their own condition.

Like the diabetic patient, these patients are given the responsibility of taking care of themselves. They are made to realize that the success of their treatment depends on the fullness of their cooperation. Almost daily we receive letters corroborating our impression that these patients have learned their lessons well and are profiting from the time spent in learning how to take care of themselves.

Progress in the treatment of peptic ulcer is inevitable if facts of known etiologic importance are utilized more fully and if, by teaching these to the patients, more intelligent and thorough cooperation is enlisted.

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THE MECHANISM OF THE EFFECT PRODUCED BY TRANSFUSED BLOOD IN SURGICAL AFFECTIONS*

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The mechanism of the effect produced by transfused blood is usually considered from five different standpoints and it is customary to speak of its substituting, hemostatic, immunobiological, disintoxicating and stimulating actions. A more thorough knowledge of the subject gained within the past few years has led to a further subdivision of these phenomena. The present paper does not deal with the mechanism of the effect produced by transfused blood in general, for the problem has been discussed in detail in the papers published by Bogomolets and his school, but is devoted to an analysis of its mechanism in connection with the various indications for blood transfusion.

We fully realize the difficulties connected with an attempt to introduce clarity into this subject and are quite ready to assume that the following concept will not be a final one.

I. THE MECHANISM OF THE EFFECT PRODUCED BY TRANSFUSED BLOOD IN HEMORRHAGE

The cause of death from hemorrhage is the acute oxygen-want to which the ganglia of the central nervous system and the automatic centers of the heart are subjected and which brings about paralysis of the respiratory center and of the heart. This sequence in the loss of functions develops with definite regularity and has been revealed in the experiments conducted in our Institute by I. R. Petrov and his assistants. The issue does not merely depend on the quantity of the blood lost, but on the rate at which it is lost. The old theory suggested by Goltz, according to which death in hemorrhage is accounted for merely by the mechanical impoverishment of the vascular channels and the heart of fluid, can no longer be regarded as the main factor. The above stated biological causes seem to be of far greater importance.

Blood transfusion in hemorrhage has a substituting effect and the transfused elements of the blood take up the physiologic rôle of the blood with its oxidizing function in the first place. The nerve centers and the cardiac

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ganglion are again supplied with blood containing oxygen, and the vascular channels are refilled with fluid. Simultaneously the other effects exerted by transfused blood also become manifest. The powerful hemostatic effect of transfused blood also makes itself clearly felt both in acute and particularly in chronic hemorrhage. The tremendous importance of *the stimulating effect* of transfused blood on the entire hematogenic apparatus in case of hemorrhage should be specially emphasized.

Seifert, Wederhake, Zeller and others lay particular stress on the rôle of blood transfusion in the treatment of hemorrhage, as a means of stimulating heart action to an extent far greater than any pharmaceutic remedy. The favorable effect of blood transfusion in cases of acute hemorrhage can be accounted for by the stimulating action on vascular tone and the removal of shock (Bogomolets). The mechanism of the action of transfused blood in hemorrhage should also be considered in the light of recent investigations on the problem of the so-called *reserve depots of blood* (Bancroft, Rein, Eppinger, Wollheim etc).

According to Bancroft, about 46 per cent of the total quantity of blood is held in reserve. These reserve depots are located in the vessels of the liver (20 per cent), of the spleen (16 per cent) and of other visceral organs, as well as in caval veins and in the subcapillary venous plexus of the skin (10 per cent). Severe hemorrhages do not exhaust the reserves of blood depots. Even in cases of a fatal loss of blood the depots are still found to contain fairly large quantities of blood (Kühl, Ratner, Tzanck, Gosset and Charrier). Transfusion is the most powerful mobilizer ("excipiens") of the blood contained in the reserve depots. These data are confirmed by clinical observations. Transfused blood does not escape from the channels of the blood vessels as do artificial solutions and, thus, the normal concentration of colloidal substances in the blood is restored.

In connection with the theory of the so-called reserve blood depots it would be more correct to speak not of the amount of blood lost, but of the degree of decompensation affecting circulation (Braitsev), of course, not in the sense in which it is customary to speak of heart decompensation, but in the sense of a redistribution of the blood in the vascular channels and the viscera.

There are certain indicators for determining this decompensation of circulation which can be used in arriving at a decision in favor of an indispensible blood transfusion.

1. *Estimation of Blood Pressure.* According to the experience gained in the world war, loss of blood was considered to be threatening to life if systolic blood pressure was reduced to below 90 mm. (maximum) and below 50 mm. (minimum). At present we believe it possible to reduce these figures down to 80 mm. There is no doubt but that the determination of blood pressure is the most reliable means of estimating decompensation of circulation.

2. *Reduction of the Number of Red Corpuscles.* According to Depage and Govaerts, loss of blood should be considered threatening if the number of erythrocytes falls below $4\frac{1}{2}$ million within the first 3 hours following the loss of blood, below 4 million in the first 6–8 hours and below $3\frac{1}{2}$ million within 12 hours.

3. *Reduction in the Percentage of Hemoglobin Contained in Blood.* Investigations conducted by Tonkes (1932) have shown the hemoglobin content of blood to fall very gradually following acute hemorrhage. The figures are usually lowest on the third day after the loss of blood has occurred. It is our belief that the determination of hemoglobin is of but relative importance as an indication of decompensation caused by acute hemorrhage.

II. THE MECHANISM OF THE EFFECT PRODUCED BY TRANSFUSED BLOOD IN TRAUMATIC AND POSTOPERATIVE SHOCK

The pathogenesis of traumatic shock has not yet been sufficiently studied and, therefore, blood transfusion has been given in such cases only on the grounds of empiric findings. Within the past few years a number of writers have published the results of their experimental investigations on the essential nature of shock, which have thrown some light on to the problem of its pathogenesis (Quen, Cannon, Crile, Keynes, Alipov, Ufreduzzi, Burdenko). Experimental investigations on the pathogenesis of shock have also been conducted at our Institute (Veselkin, Lindenbaum, Doepp and Takhibekov, 1936). The numerous data reported by a number of authors of different countries have contributed towards introducing somewhat greater clarity into the explanation of the *mechanism of the effect produced by transfused blood.*

1. Traumatic shock causes *decompensation of circulation.* A sudden and marked fall in the quantity of circulating blood occurs. The blood *flows to the reserve depots,* which for the most part are the capillaries of the abdominal cavity. The flow of blood in the capillaries is delayed (stasis) and according to some authors the plasma penetrates through the walls of the capillaries into the interstitial spaces. In this connection *an increased concentration* of the tissue elements of the blood is observed. The number of red corpuscles and the per cent of hemoglobin contained in 1 mm. are found to increase. Clinically this is manifested by a marked *fall in blood pressure* (both arterial and venous). The data obtained in our Institute (Veselkin, Lindenbaum, Doepp and Takhibekov) have failed to confirm the condensation of blood in traumatic shock and these contradictions will require further study.

Blood transfusion given in traumatic shock corrects decompensation of circulation. Mobilization of the reserve depots of the blood occurs, which results in a rapid increase in the quantity of circulating blood. Capillary "stasis" is found to abate and the plasma, as some authors

believe, returns to the channels of the blood vessels, thus lessening the concentration of blood. This is manifested clinically by an increase in the blood pressure. Contrary to substituting solutions, transfused blood does not leave the blood vessels and is therefore capable of developing its substituting properties. This complex action is of particular importance in cases of shock associated with great loss of blood.

2. The above-mentioned decompensation of circulation occurring in traumatic shock, accompanied by the redistribution of the circulating blood into the reserve depots, results in the insufficient blood supply and the *oxygen-want of the ganglion cells of the central nervous system and of the heart*. This causes all the cells of the organism to be affected with acidosis, due to insufficient circulation.

When blood transfusion is given, the mobilization of the blood in the reserve depots and the increase in the general quantity of circulating blood *does away with the oxygen-want of the central nervous system and of the* heart, as well as with the acidosis of the cells, and the normal conditions of metabolism are restored. Hyperglycemia is found to disappear (Banaitis) owing to the action of transfused blood on the brain function and to its regulating effect on disturbed metabolism (Bogomolets). Besides this normalizing effect produced by blood transfusion on the tone of the nervous and the vascular systems, *the vasomotor properties peculiar to transfused blood itself* should also be taken into account (Rasenkov).

And, finally, some authors also take into account *the disintoxicating action of transfused blood* which *neutralizes toxemia* caused by the absorption of protein products from the blood plasma that has penetrated into the tissues in the areas affected by capillary stasis (The English Shock Commission). Our experimental investigations have failed to confirm the intoxication hypothesis of traumatic shock and therefore we still are doubtful of the point of view that the disintoxicating action of transfused blood is the leading factor in traumatic shock.

III. THE MECHANISM OF THE EFFECT PRODUCED BY TRANSFUSED BLOOD IN CHOLEMIA AND ACHOLIA

The mechanism of blood transfusion in cholemia and hemorrhages, the pathogenesis of which has not yet been sufficiently studied, is naturally somewhat vague. Bauer, Lüdke, Fenyvessy and Ponder have proved the disintoxicating action of blood serum on bile acids. Freund and Rasenkov emphasize the vasoconstricting effect of transfusion, which resembles that of adrenal. According to Beczeller and Schönbauer, transfusion supports the disintoxicating rôle of the liver. Elansky lays stress on the fact that transfused blood introduces simultaneously *vitamins, excessive calcium* and nutrient substances. The extra- and intracellular processes of assimilation and dissimilation are restored to normal and the coagulability of blood is increased.

IV. THE MECHANISM OF THE EFFECT OF TRANSFUSED BLOOD IN AMBUSTION

The mechanism of blood transfusion in ambustion may be accounted for in the following way.

1. The *shock* observed either directly after, or within, the first 24 hours following severe burns is best alleviated by transfusion, the mechanism whose action has already been discussed. In this case the decompensation of circulation is eliminated and mobilization of the reserve blood depots occurs. Capillary stasis is removed and the plasma returns to the channels of the blood vessels. This results in increasing blood pressure and decreasing blood concentration.

Ambustion is followed by a marked rise in the number of erythrocytes which sometimes reaches up to 7 million, in an increase in the blood content of hemoglobin, in an increased number of leucocytes, up to 35,000, in a rise in the dry residue of the blood, in a fall in the chloride content of the blood down to 300 mgm. per cent (Spasokukotsky and Braitsev). The observations carried out at our Institute by Lindenbaum and Bogomolova have confirmed the development of such phenomena as blood concentration, increase of erythrocytes up to 5-6 million, rise in the hemoglobin content up to 100 per cent and over, and of the number of leucocytes up to 16,000. Besides, the coagulability of blood is increased (hemocoagophilia) and the quantity of urine passed daily falls to 200-300 c. c.

Following blood transfusion a noticeable *decrease in the condensation of blood occurs, its coagulability approaches normal and the quantity of urine, passed daily, increases.*

Contrary to substituting solutions, transfused blood does not escape from the vascular channels; it not only eliminates the above-mentioned symptoms of shock, but also *replaces the erythrocytes,* which perish in the second period of ambustion, and *acts as a stimulant* on the hemogenic apparatus.

2. Owing to the oxygen-want affecting the cells of the central nervous system, of the heart, and of the whole of the organism, acidosis is reduced and metabolism is found to improve, which to a certain extent compensates for skin respiration.

3. In the second stage of ambustion, when the phenomena connected with the organism being subjected to intoxication with the protein products of decaying tissues set in, blood transfusion may be supposed to have a disintoxicating effect.

V. THE MECHANISM OF THE EFFECT PRODUCED BY TRANSFUSED BLOOD IN INTESTINAL OBSTRUCTION

The benefit of blood transfusion in intestinal obstruction is due to *disintoxication.* Ileus causes the ganglia of the central nervous system and of those of the heart to be poisoned with toxins absorbed from the

intestine. Blood transfusion, apparently, results in the toxins being adsorbed by the erythrocytes of the transfused blood, which contribute towards inactivating the poison and removing it from the blood plasma of the recipient (Lintvarev, Spasokukotsky). In intestinal obstruction death is due to intoxication and dehydration. Transfusion ofttimes proves to be a successful means of fighting both these factors. In addition, a fall in the content of chlorides is also effected by it (Seltsovsky, Tsipk, Samarin and his collaborators). Seltsovsky has succeeded in proving that, as compared to blood transfusion, substituting solutions given in ileus are practically of no avail. Out of 11 dogs experimented upon by Seltsovsky only 3 survived after obstruction had been removed and they had received infusions of normal saline solution. Out of 7 other dogs which had been given blood transfusion, 6 animals survived and only 1 died of peritonitis. In all the dogs the percentage of chlorides was reduced to normal within 3 days.

VI. THE MECHANISM OF THE EFFECT PRODUCED BY TRANSFUSED BLOOD IN GENERAL PURULENT INFECTION

See Hesse "Blood Transfusion in General Purulent Infection" Vestnik Chirurgii, 51, N. 5, 1937.

VII. THE MECHANISM OF THE EFFECT PRODUCED BY TRANSFUSED BLOOD IN CASES OF POISONING

The mechanism of the effect of transfusions in poisoning is based on the disintoxicating action of transfused blood. Transfusion can be expected to have the desired effect in all cases of poisoning in which the poison is found to circulate in the blood and in which a certain *dilution* of the poison can be achieved by means of giving a transfusion. Success is probable in dealing with poisons which change the chemical composition of hemoglobin with the result that the latter is converted into carboxyhemoglobin (carbon monoxide, illuminating gas) metahemoglobin (anilin, phenols, nitrites etc.) and cyanhemoglobin (compounds of hydrocyanic acid).

Successful results may be possible in dealing with poisons causing hemolysis of the blood (saponin, aspidin, compounds of arsenic, mushroom—poison and venom, etc.). Least of all one might expect to obtain the desired effect in cases affected with protoplasmatic poisons of a *globulicidal nature*.

The problem of efficiently diluting poison circulating in the blood by giving intravenous injections of solutions of blood has not yet been finally solved by modern toxicology. The poison is unequally distributed within the organs and the cells of an organism, depending upon the affinity of the poison to the different tissues. The effect produced by the poison is not in proportion to the amount of poison introduced into the organism. And, finally, estimations of the dilution of the poison which can be attained by means of blood transfusion have proved its possibilities to be

relatively insignificant. At best, blood transfusion decreases the concentration of poison in the blood by one-tenth (Merke, 1935).

These considerations have long since given rise to the idea of preceding transfusion by bloodletting. "Exsanguination Transfusion," as it has been termed by American and English authors, has been known for a long time. Lesser administered it in ambustion in 1880; Robertson recommended it for the treatment of toxemia in 1924; and Henschen administered it in toxicosis caused by Basedow's disease in 1927.

At present bloodletting is believed to be indicated in connection with blood transfusion in any case of poisoning. Unfortunately, however, bloodletting also effects but an insignificant dilution of the poison circulating in the blood. According to Merke's calculations, if the general amount of blood is 5 litres, and 1 litre of blood is let, and 1 litre given in transfusion, the poison is found to be diluted at best by one-fifth, and its concentration changed by one-fourth. These calculations are not quite correct in the sense of a general estimation of the effect of blood transfusion because the disintoxicating action of transfused blood does not merely consist in mechanically diluting the poison but in *drawing the poisonous products away* from the red corpuscles and in the *substituting* and *stimulating* effects. Therefore, there is every reason to believe blood transfusion to be an excellent remedy in all cases in which there is a subsequent anemia.

It follows from the above statements that blood transfusion given in cases of poisoning should be regarded as a rational method of treatment. In acute poisoning bloodletting should be resorted to and large doses of blood should be given in transfusion. In the event of the effect being insufficient, both bloodletting and transfusion should be repeated. Blood transfusion belongs to that class of methods in which empirical practice has left theory far behind. The scientific foundation of this most valuable method of treatment was laid much later. Even at present, not nearly all the questions connected with the mechanism of the effect produced by transfused blood have been finally answered.

Here the problem is considered as it is seen in the light of the present day and there is no doubt that a great deal still remains to be said on the subject and that many things which are not quite clear as yet will find an adequate explanation in the future. Opportunities for the further development of the problem of blood transfusion should be sought not in an attempt to find other pathologic conditions for the administration of blood, but rather in a more thorough study of the action of transfused blood. It will then surely prove possible to establish additional affections in which blood transfusion will be found to be indicated.

SUMMARY

The writer offers the present point of view on the problem of the mechanism of the effect produced by transfused blood in various surgical affections. In cases in which loss of blood has occurred blood transfusion

acts as a substitute. The nerve centers and the heart ganglion are relieved of the condition of anoxemia and the vascular channels are refilled with fluid. Alongside this the hemostatic and the stimulating effects of transfused blood also make themselves felt. It also stimulates the heart and raises the vascular tone more efficiently than any pharmaceutic remedy. Blood transfusion causes the *mobilization of the reserve depots of blood.* Based on the theory of the reserve depots of blood it should appear to be more correct to speak not of the amount of blood lost, but of the condition of decompensated circulation. The most important factor in estimating decompensation is blood pressure.

Decompensation, i.e., a pathologic redistribution of blood, is also the first symptom which is eliminated by blood transfusion in traumatic and postoperative shock. This corrects the anoxemia and the acidosis, affecting the cells of the entire organism. The vasomotor properties of transfused blood should also be taken into consideration.

In cholemia transfused blood may be supposed to have a disintoxicating effect on the plasma and owing to its adrenal-like properties produces a vasoconstricting effect. It also introduces large quantities of calcium and vitamins.

In ambustion the main rôle of transfusion lies in overcoming the shock. In the second period in which large numbers of erythrocytes are destroyed, the substituting and stimulating action of transfused blood has also to be taken into account. Its disintoxicating effect reduces the intoxication caused by the protein products of decaying tissues.

In intestinal obstruction as well, the most important factors are the disintoxicating effect of transfused blood and its capacity for reducing dehydration. The same disintoxicating action is of paramount importance in cases of poisoning. Blood transfusion reduces the concentration of the poison by one-tenth; if combined with bloodletting by one-fifth. However, its effect does not merely consist in diluting the poison, but in drawing it away from erythrocytes.

SUPERNUMERARY CERVICAL RIB

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The relatively rare occurrence of the supernumerary cervical rib has induced me to present this work with the description of the surgical technique used in its treatment, bringing forth also some anatomic and embryologic details of importance in relation to this anomaly, contributing in this way to the testimonial recognition tendered to Doctor Richard Lewisohn.

Though some of the ideas which I express have already been discussed by me elsewhere, a new operation which I performed last March on one of my patients has impelled me to complete this matter and to express my views on the treatment of this deformity.

The supernumerary cervical rib has been a known deformity since the era of ancient medical history; the improvement in radiologic technique has lately multiplied the number of cases reported. While in the cases presented there were sufficient objective and subjective symptoms to warrant a clinical diagnosis, in 90 per cent of patients in general cervical rib does not produce symptoms and only an X-ray examination of the chest, performed in the course of some other investigation, discloses the presence of this bone anomaly.

CASE RECORDS

Case 1. This case was treated for the first time in September 1931. The patient, J. V., a young Cuban woman, white, 20 years of age, stated that for two years she noticed nervous and vascular disturbances in the left upper limb, consisting of cyanosis, cramps and pain radiating to the back. This symptomatology had lately increased in intensity. Personal and hereditary data were without significance. An appendectomy had been performed by me in 1929.

Examination. A hard tumor was noticed in the left supraclavicular region. It was painless, slightly prominent and elongated anteroposteriorly. Her blood pressure was 115 systolic and 85 diastolic in the right arm; 95 systolic and 70 diastolic in the left arm.

With these physical manifestations and the subjective symptoms as given by the patient, the diagnosis of a left supernumerary cervical rib was made and was verified by X-ray investigation (Fig. 1). The X-ray report

by Dr. Padron read as follows "Supernumerary cervical rib; increased in volume in the middle portion of its arch in a spindle-like fashion; at that level there is a zone of greater transparency formed by incomplete ossified bone; small incomplete rib on the opposite side."

Course. The urine, blood and respiratory and circulatory systems were duly investigated and the patient was operated upon by me on October 2, 1931 and, according to the technique of Adson (Mayo Clinic), with the use of nitrous oxide anesthesia the tendon of the scalenus anticus at the level of its insertion in the first rib was sectioned.
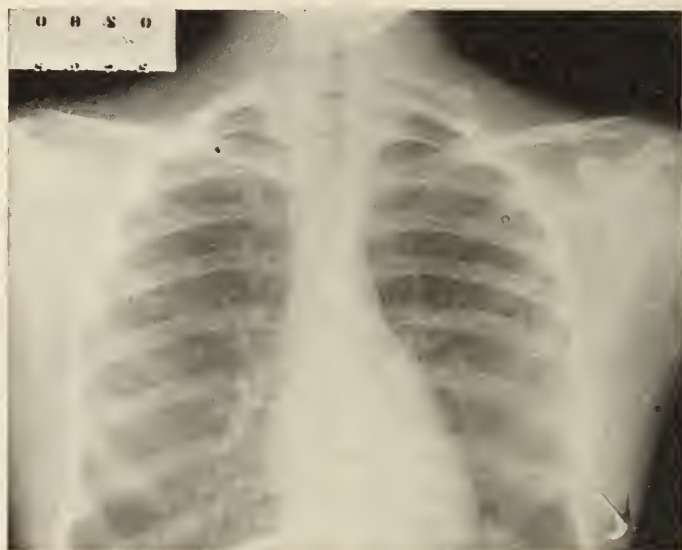
Fig. 1. J. V. Supernumerary cervical rib, increased in volume in the middle portion of its arch in a spindle-like fashion; at that level there is a zone of greater transparency formed by incomplete ossified bone; small incomplete rib on the opposite side. Dr. Padron, radiologist.

Comment. The symptoms exhibited by patients who suffer from this anomaly are mostly due to the pressure exerted by the scalenus anticus on the subclavian artery and transmitted through it to the nerve filaments of the brachial plexus which, as a result, are pressed against the cervical rib. Naturally, if one of the pressing agents is removed, pressure will disappear. It is for this reason that in the present case section of the tendon of the scalenus anticus was performed.

The patient made an uneventful recovery with the disappearance of all pressure symptoms. With the blood pressure recorded as 120 systolic and 80 diastolic in both arms she was discharged on October 10, 1931. Two years later there was a recurrence of the symptoms with dyspnea and dysphagia. The blood pressure was 125 systolic and 75 diastolic in the right

arm and 120 systolic and 70 diastolic in the left arm.   A new X-ray exami-
nation again showed the same results as reported previously.

With a recurrence of all the pressure disturbances we had to admit that
either some posterior fibers of the scalenus anticus had been left unsec-
tioned or that the rib kept on developing and exerting pressure, this time
against the cicatricial fibrous tissue and the soft tissues of the neck.   Dr.
Adson was consulted, setting forth his points of view in harmony with our
suspicion and an operation was performed in June 1934 which I shall
describe in Case 3.

Case 2.   I. S. from Cuba (mestiza) half Indian, married, 38 year old
seamstress, was referred to me at the surgical service of the Hospital de
Emergencias (Emergency Hospital) by my assistant, Dr. Armstrong, in
order to obtain my opinion as to the presence of a tumor in the left supra-
clavicular region.   This tumor was slightly prominent, hard, painful,
fixed, throbbing and elongated anteroposteriorly towards and up to the
spinal column.

The patient stated that two years previously she had noticed a small
tumor with painful sensation at that level and that both symptoms had
increased steadily in intensity since that time.   With the suspicion of
supernumerary cervical rib, the presence of circulatory and vascular dis-
turbances at the level of the left upper limb was investigated but with
negative results.   X-ray examination, however, confirmed the diagnosis
of left complete cervical rib (Fig. 2).

Course.   The urine, blood and respiratory and circulatory systems were
examined and found negative.   The blood pressure was 105 systolic and
65 diastolic in both arms, the pulse being 88 per minute.

Bearing in mind our experience with Case 1, I decided to perform the
complete resection of the cervical rib by the transbrachial approach;
though more difficult and elaborate, it gives more satisfactory and definite
results in the treatment of this anomaly.

Operation.   Anesthesia: avertin, by Dr. Dominguez Avila, on May 16,
1934.   The head of the patient was rotated towards the sound side and at
the same time the stump of the shoulder was pulled downwards and back-
wards in order to expose the organs of the region.

Technique.   Paraclavicular incision of Adson (Fig. 3) through skin and
subcutaneous cellular tissue (cutaneous muscle of the neck) is made.   The
superficial cervical aponeurosis is exposed, the omohyoideus and the exter-
nal jugular vein grasped between two forceps and the cervical aponeurosis
incised.   There now appears in the operating field the scalenus anticus
with the phrenic nerve resting on its anterior surface, crossing it obliquely
from the external to the internal border, which it reaches at the point where
the scalenus anticus meets the tuberosity of Lisfranc.   Turning the
phrenic nerve inwards and upwards and the superior scapular artery down-
wards (this vessel being a branch of the subclavian which runs parallel

across the superior border of the clavicle), the terminal tendon of the scalenus anticus is sectioned through its whole thickness as near as possible to its costal insertion. Immediately the muscular mass of the scalenus anticus contracts upwards and leaves exposed the supraclavicular space with the subclavian artery and the nerve filaments of the brachial plexus resting on the cervical rib (Fig. 3). The artery is liberated through careful dissection, as are also the anterior roots of the seventh and eighth cervical nerves and the first dorsal nerve, thus avoiding injury to the vertebral and inferior thyroid arteries (branches of the subclavian which, running upwards vertically from their point of origin, rest in the medial

Fig. 2. I. S. Left supernumerary cervical rib. Drs. Sanchez, Pesino and Busquet, radiologists.

portion of the transverse apophysis of the last cervical vertebra). This step performed, the seventh cervical nerve is lifted upwards and backwards and the inferior roots are brought downwards, freeing in this way the posterior third of the supernumerary rib at its junction with the spinal cord. Separating then, upwards and backwards, the inferior trunk of the brachial plexus, and bringing the subclavian artery inwards and forwards, we are in position to liberate the rest of the osseous anomaly in its entire extent, being careful not to perform too drastic an elongation of the nerve roots in order to avoid paresis and postoperative neuralgia.

With the scalpel an incision through the periosteum along the superior border of the rib is made, separating it with the periosteotome from the

whole osseous surface; this precaution has the advantage of protecting with greater safety the pleural apex which at times adheres firmly to the cervical rib (Adson). A gouge forceps is utilized in the procedure of resecting this anomaly thoroughly.

When, as in the present case, a fourth degree rib of Andrews is discovered, that is, a complete rib which ends in the anterior extremity of the first thoracic rib, the disarticulation or disconnection of this union (in order to facilitate the resection of its posterior extremity in the cervical column) is the first step to be performed.

With the operating field free of the supernumerary rib, it is easier to separate the periosteum from the pleural apex; after this step is made

Fig. 3. Incision of Adson.

and when it is found that there are no osseous prominences on both surfaces, then the different layers of tissue are closed and the operation is completed.

The patient had an uneventful recovery and was discharged eleven days after the operation.

In March 1937, three years after the operation, this patient was again examined; the scar was almost invisible and there was no supraclavicular tumor and no pressure symptoms. Another X-ray examination showed the complete disappearance of the supernumerary cervical rib (Fig. 4).

Case 3. J. V., whose history and first operation were described previously, was again operated upon on June 25, 1934 at Clinica Fortun Souza.

Operation. Anesthesia: avertin. The scalenus anticus was exposed and

it was found that some posterior fibers of that muscle had not been sectioned at the first operation. As soon as they were incised, it could be noticed that the vascular and nervous compression exerted upon the cervical rib came from the point of union between this and the first thoracic rib and for that reason the osseous anomaly was removed (resected) in accordance with the technique described above. In the present case the whole rib was not resected as in Case 2. The operative difficulties encountered, due to the shortness of the neck of this patient—and also because of the point of view I held earlier that it was not absolutely necessary to resect the entire rib (believing as I did in the absolute freedom of the vessels and nerves in the region in question after the section of all the fibers of the scalenus anticus, as well as those of the cicatricial bands),—induced me to perform an incomplete resection of the anomaly.
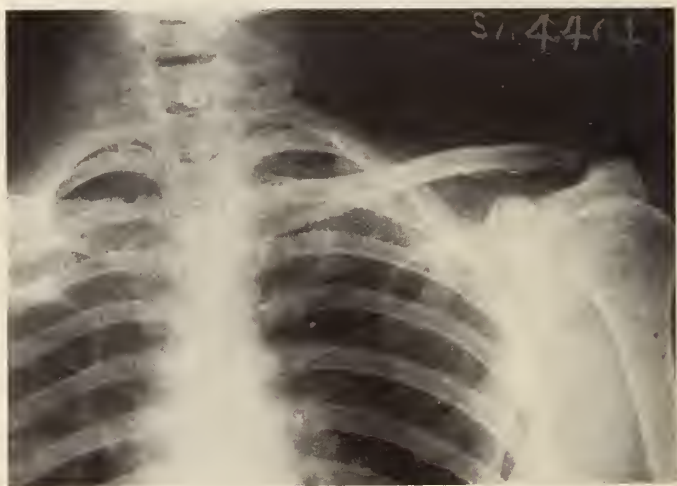
Fig. 4. I. S. Left cervical rib, totally resected.

During the postoperative period a moderate painful sensation was experienced by the patient in the left upper limb, but it yielded to the usual analgesics. The patient was discharged, improved. ten days later.

In view of the fact that symptoms did not disappear completely, I kept on observing the patient regularly. A few months later her disturbances increased in intensity and the former clinical picture made its appearance again. During the following two years her condition grew worse. She had hypothermia and pain along the arm, edema and sensation of traction in the supraclavicular region and left shoulder, painful motion in the shoulder and upon rotation of the neck, with the final development of a marked degree of atrophy in the left upper limb. X-ray examination showed only partial resection of the osseous anomaly. Massage, heat and diathermy did not improve her symptoms.

At this stage a new operation was performed by me on March 2, 1937, with the efficient cooperation of Dr. Sauchez Toledo.   I made a complete resection of the remnants of the cervical rib, as shown in Figure 5, and also removed all the cicatricial bands which exerted pressure upon the vessels and nerves of the region.   After eight days she was discharged, very much improved.

At present, after six weeks, the patient feels very well; she has gained fifteen pounds in weight; her painful sensations have disappeared; she can move her neck, shoulder and arm in all directions; the circulation in the arm has been reestablished with initial correction of muscular atrophy and

FIG. 5. J. V. Left cervical rib completely resected.

return of muscular function; the supraclavicular region is painless and, in general, it can be stated that the result of the operation has been perfectly satisfactory.

COMMENT

The supernumerary cervical rib is an affection more common in women than in men and is bilateral in 75 per cent of the cases.   Though it originates usually in the seventh vertebra, cases are on record with its origin in the sixth and even in the fifth cervical vertebrae.

Crouzon (1923) and Leri (1924) in the Presse Medical were the first who made a thorough study of this matter, not only from the clinical and anatomical viewpoints, which I shall discuss later, but also from the point of view of embryology.   They defined the constitution of the supernumerary ribs as both lumbar and cervical.

We know that in the adult each rib is composed of head, neck, tuberosity and body, articulating by the head with the bodies and intervertebral discs and by its tuberosity with the vertex (apex) of the transverse process apophysis. In the early days of embryonic life all the vertebrae, with the exception of the coccygeal, have their pair of rudimentary ribs represented by a small cartilaginous arch; later those of the cervical region are reabsorbed, as well as those of the lumbar and sacral regions.

These primitive ribs, articulate only with the transverse process, have neither head nor neck, and are called diapophysiary ribs. Later on, there appears a cartilaginous disc which unites on one aspect with the tuberosity of the rib and on the other with the vertebral bodies, giving rise to the head and neck. This is the parapophysiary or capitular portion of the primitive rib.

The knowledge of these processes leads to the differentiation of the two types of supernumerary ribs. If the reabsorption of the primitive cartilaginous arches does not take place in some lumbar or cervical vertebra, it gives rise to the presence of a supplementary rib which begins at the level of the extremity of the transverse process. As this rib lacks a head and neck, being represented only by its body and tuberosity, it receives the name of (tubercular) diapophysiary supernumerary rib. If, on the other hand, the lumbar or cervical cartilaginous nuclei (being unable to join the ribs, as they do not exist at that level, and also unable to join the vertebral bodies), disappear as independent nuclei but articulate with vertebral bodies at the level of the thoracic segments, they give rise to another and different type of supplementary rib, with a smaller head and neck, much shorter than those previously described, and hardly as long as the transverse process. These are the parapophysiary or capitular supernumerary ribs. In the last instance there exists a mixed type which is both tubercular and capitular, articulating with the transverse processes and with the vertebral bodies and having a head, neck, tuberosity and body like a thoracic rib in the adult.

Frequently the disturbances which they produce are not in harmony with the size of the rib. Mouchet and Gastaud described a case (Societé de Chirurgie de Paris, July 9, 1924) of bilateral supernumerary rib wherein the disturbances were more marked on the side of the shorter rib.

Symptomatology. Although I have already mentioned the absence of subjective symptoms in the majority of persons who have this anomaly, in 10 per cent of the cases there appear disturbances of two types, namely, nervous and vascular in the superior limb or locally.

The most frequent nervous symptoms are: pain upon pressure and also spontaneously in the supraclavicular fossa; and anesthesias, paresthesias, or neuralgias of the upper extremity on the same side. Less frequently the cervical sympathetic and the recurrent nerves may also be compressed,

giving rise to their specific symptoms, namely, lacrimation, disturbances of vision, hoarseness and dysphagia.

The vascular symptomatology depends upon the compression of the subclavian artery. An arterial impulse is noticed above the clavicle; the circulation in the superior limb is deficient; there is local anemia, weak radial pulse or even absent pulse and in these cases the circulation is established through collateral channels. At times this is insufficient and dry gangrene develops in the tips of the fingers. Symptoms due to compression of the subclavian vein are rare, but in some cases there is edema of the superior limb resulting from deficiency of the return circulation.

In regard to the appearance of the initial symptoms, I might say that there are two age periods in the life of a person wherein their appearance is more common, namely, from 20 to 25 and after 50. In order to explain the first age period, Professor Dubreuil-Chambardel reminds us of the process of ossification of the vertebral column which, so far as we know, is completed at the ages of 20 to 22 years. During the first years of life vessels and nerves rest on comparatively soft tissue, but later on the osseous system becomes hard and rigid and active motion makes the muscles hard and voluminous; the vessels and nerves are definitely fixed between rigid planes and firm organs which transmit to them all their movements and pressures. It is at this time that the first vascular and nervous pressure symptoms appear. Other authors like Crouzon and Chaumet explain the appearance of late manifestations as the result of added spondylitis which exerts pressure on the cervical roots or as due to an exaggerated curvature of the spine at that age which brings a closer contact between the rib on one side and the nervous roots and blood vessels on the other.

Other cases have been reported wherein the appearance of the symptoms has been related to the profession or trade of the patient. Quervain of Berne reports the case of a soldier who suffered from this anomaly as the result of the pressure exerted by a Sam Browne belt on the shoulder which interfered with the circulation to such an extent that the radial pulse disappeared. Such patients are benefited by rest and change of occupation to the point where their disturbances may disappear. For the others, as in the cases previously described, no other causes can be determined except the pressure exerted by the growth of the osseous anomaly on vessels and nerves and they do not have, in my judgment, any other successful treatment but the complete resection of the supernumerary cervical rib.

MECHANISM OF THE REACTION OF SUBSTITUTION AND WALDEN INVERSION

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In order to test recently-advanced theories of the mechanism of the reaction of substitution claiming that every substitution by a negative atom or group takes place on the positive end of a dipole, experiments were instituted based on the following considerations.

A single reaction of substitution on an optically active carbon atom should lead to inversion of configuration and two consecutive reactions of substitution should lead to a substance having the configuration of the starting substance. From work done in our laboratory, the conclusion was reached that secondary normal aliphatic alcohols and the corresponding amines rotate in the same direction. Evidence also was furnished in our laboratory that the three corresponding chlorides, bromides and iodides rotate in the same direction. For the solution of our problem a system was selected leading from the alcohol to the amine through the intermediary of a halide.

The result from I to IV or from I to VI is due to two consecutive reactions accompanied either with or without inversion of configuration but the result from II to V is definitely due to a reaction connected with an inversion of configuration. Inasmuch as chemically the azido group behaves like a halogen, it may be assumed that on substitution it will approach a dipole from the same side as a halogen atom and therefore it may be assumed that the reaction from II to III is connected with an inversion. Consequently, the reactions leading from I to IV include two reactions of substitution, each connected with inversion. It would follow also that the reaction from II to VI is accompanied with inversion.

On the basis of the postulate of similarity of the behavior of the azido group and of the halogen atom, it may then be assumed that in the group of normal saturated secondary alkyl derivatives all reactions of substitution by a negative group or ion are accompanied with inversion of configuration and hence in this group of substances all substitutions take place on the positive end of the dipole.

On the contrary, when R_1 is an unsaturated radicle $(-CH=CH_2-)$ or when $R_2 = -C_6H_5$, then two consecutive reactions of substitution may lead to a substance having a configuration opposite to that of the starting material, thus showing that only one substitution is accompanied with inversion of configuration, the other without. Hence, one substitution

by a negative ion takes place on the positive, the other on the negative end of the dipole.

$$R_1 \\ | \\ H—C—Cl \\ | \\ R_2$$

dextro

V

$$R_1 \qquad\qquad R_1 \qquad\qquad R_1 \qquad\qquad R_1 \\ | \qquad\qquad | \qquad\qquad | \qquad\qquad | \\ H\cdots C\cdots OH \xrightarrow[\odot]{HI} I—C—H \xrightarrow[\odot]{KN_3} H\cdots C\cdots N_3 \xrightarrow{H_2 + Pt} H\cdots C\cdots NH_2 \\ | \qquad\qquad | \qquad\qquad | \qquad\qquad | \\ R_2 \qquad\qquad R_2 \qquad\qquad R_2 \qquad\qquad R_2$$

dextro   levo   dextro   dextro

I   II   III   IV

$$R_1 \\ | \\ H\cdots C\cdots NH_2 \\ | \\ R_2$$

dextro

VI

$(R_2 > R_1)$
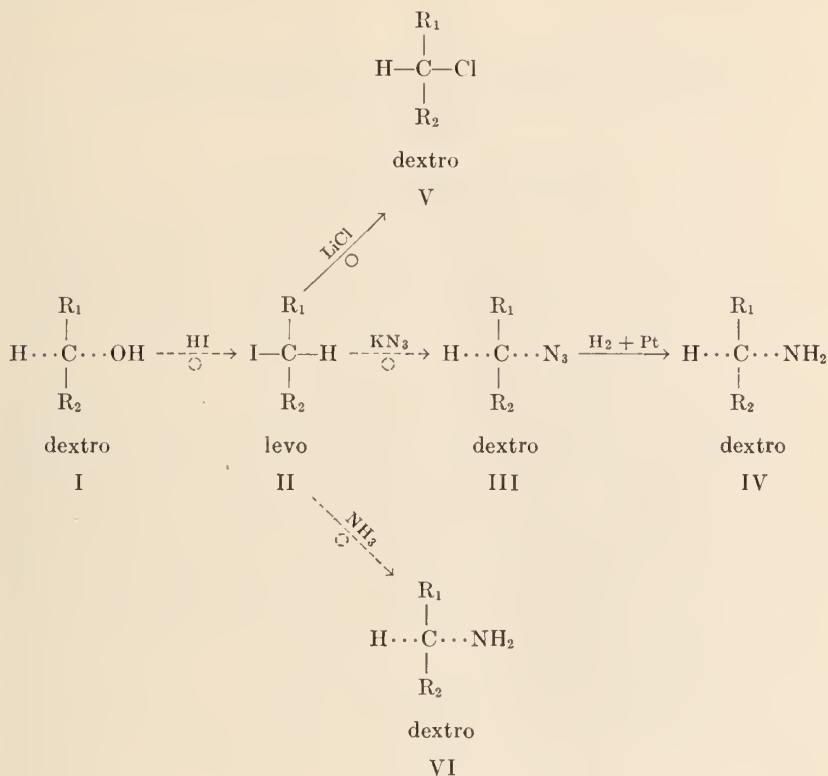
One of the chemical differences between the two groups of substances consists in the difference in the velocities of substitution. Thus the outcome of a reaction of substitution is somehow associated with its velocity. This assumption was made several years ago by the present authors and was later arrived at by several other investigators.

It may be mentioned that in some of the substances in which a reaction of substitution was found to take place without inversion, it was possible, by changing the external conditions of the reaction, to cause the reaction to proceed with inversion. There is hope, therefore, that detailed study of the dynamics of the reaction under different external conditions may bring more light toward the solution of the problem of the mechanism of the reaction of substitution.

TRANSFUSION BY LEWISOHN'S CITRATE METHOD: THE FIRST CASE IN A HUMAN BEING IN NORTH AMERICA

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The following case is here presented not merely as a clinical report, but with a few words of personal recollection of modern blood transfusion. I say modern, because it is well known that attempts were made centuries ago to introduce alien human blood into the human circulatory system. These were all failures and, I think, resulted fatally. Not until the discovery that the circulating blood in human beings was not of the same exact physiological character in all individuals, did transfusion promise any method worth developing. Dr. Karl Landsteiner of the Rockefeller Institute, Nobel Prize winner, was able to divide the blood of human beings into four main groups of compatibility, although we now know that certain of these groups are compatible with others not of their exact type. Thus, for example, we may have universal donors or universal recipients, reminding one of a master-key for locks. Those interested can easily gain access to the numerous publications on the subject.

My first transfusions were accomplished by direct suture of the radial artery of the donor to a vein, usually in a patient's arm. Carrel had done this successfully, one of the few times when he acted as a surgeon for human beings—the patient, the newborn child of one of his friends, who was himself a surgeon. In my hands this form of transfusion was almost invariably successful, but, of course, there was the disadvantage of not knowing exactly how much blood entered the patient's circulation. One had to judge by the appearance and by the character of the recipient's pulse. It was Carrel's technique which I employed. The local anesthesia (cocaine) which was used, contracted the radial to such a degree that my fingers, less skillful than those of Carrel, were sorely taxed by the delicate manoeuver. Later, it was Dr. Crile, I believe, who invented the vein-to-vein suture method which was a decided advance in technique. Even here, however, the procedure was a very delicate one, and the tendency to coagulation was greater than in the artery-to-vein method.

Then came the various forms of cannula, Dr. Charles A. Elsberg having been among the first to present a satisfactory instrument. But even here there were annoyances, coagulation and difficulties of application, especially when the veins were small. Finally a great advance was made by Dr. H. Lindemann who employed from six to ten 20 c. c. syringes, rapidly

drawing blood from a needle or cannula in the donor's vein, and then injecting it into the vein of the recipient. This required at least one assistant whose place it was to keep these syringes in working order during the transfusion. The results were good. However, it remained for Dr. Lester Unger to devise an appliance with valves so that only one syringe was necessary. He showed me his first, unfinished model of this apparatus, and I was inclined to discourage him, for I did not see how it could be possible that the blood would remain fluid in its complicated course from the donor to the patient. My opinion did not discourage Unger, however, and his results were brilliant. His method has come to stay.

I have mentioned only a few of the technical devices for direct transfusion. It was not until Lewisohn conceived the idea of preventing blood-clotting outside the body without previous defibrination, that this important life-saving measure was put into the hands of the profession. I need not describe the citrate procedure, because Lewisohn has done it so well himself and his papers are within easy reach. The first time it was done in North America, and probably the first anywhere, will now be reported.

The patient was a man about fifty-five years old, Barnett F., who had suffered from weakness and anemia for about two years before I saw him. He stated however, that he had entirely recovered from this disease of the blood. Then his symptoms recurred and on admission to the hospital he was profoundly anemic, and no cause for this had been discovered. He had been under the care of numerous physicians and surgeons. He had been under observation at the Presbyterian Hospital. It was Dr. Elsberg who, in December 1914, had concluded that the man was probably suffering from a carcinoma of the stomach, a diagnosis which to him appeared confirmed by the X-ray plate. I saw the patient first on January 25, 1915. A few days before, Dr. Hooker had transfused 250 c. c. of human blood, using the syringe method. A chill had followed this procedure, with the rise of temperature to 104°F. There was great prostration and aggravation of the anemia! He was very weak and it did not seem that he could live many days. I then suggested another transfusion, this time by the sodium citrate method, and the patient was transferred to The Mount Sinai Hospital (Gen. Surg. 40–10, 1915).

Here a careful examination revealed a Virchow's lymph node with surrounding induration in the left supraclavicular region, and it was my idea that this should be removed for diagnostic purposes. On January 26th I transfused 700 c. c. of blood by the citrate method, and the signs of immediate improvement were startling. This was subjective as well as objective, the patient even stating that he felt perfectly well. Then, at the same sitting, I removed a portion of the supraclavicular mass, and, in doing this, the dissection had to be carried down almost to the pleura. There was no abnormal bleeding, nor was there subsequent disturbance of any kind; no chill. In twenty-four hours Dr. Fred Mandlebaum, pa-

thologist to the hospital, reported carcinoma, but he was unable to state whence the metastasis may have come. I believed, however, that the diagnosis of gastric carcinoma was sufficiently clear. Two days later the patient was discharged, his general condition greatly improved. There was no subsequent surgical procedure upon the stomach.

The ease and simplicity of this transfusion was most amazing to me, who had so often suffered more than the patient in performing this life-saving operation.

LYMPHANGIECTATIC ENVELOPE OF THE SMALL INTESTINE CAUSING CHRONIC MEMBRANOUS OBSTRUCTION

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Two cases of an unusual affection of the small intestine are presented, with the term *lymphangiectasia* used in order to convey some understanding of the pathological findings at operation, although it barely does justice to the clinical condition.

In the two cases incomplete obstruction of the small intestine was caused by a peritoneal membrane embracing within its folds a large segment of the small intestine. Surgical release of the membrane resulted in restoration to health.

There is no description in medical literature that explains the anatomical findings encountered at operation. The extreme rarity of this condition is evidenced by the fact that only two cases have been seen in our combined experience, which covers the best part of a generation, in which attention has been devoted to unusual intra-abdominal diseases and abnormalities. The clinical histories, in brief, are as follows.

Case 1. History (A. H., Gen. Surg. 34-28, 1923). A 51 year old machinist was seen for the first time in 1923. He was an active worker with no previous illnesses, except for a left inguinal herniotomy one and one-half years previous to admission. For six months he had experienced epigastric pains after eating. Severe abdominal cramps, lasting for as long as ten hours, followed a heavy meal; these were relieved by vomiting. The vomitus contained food and bile but no blood. The attacks occurred usually at night, following a meal at the end of the day's work and at about two-week intervals. The pain was felt with the greatest intensity in the epigastrium; it radiated over the whole abdomen and referred to the back. His appetite was fair. The patient suffered from slight constipation. He had lost ten pounds during the six months of active symptoms. His eating habits were good. There were no symptoms referable to other visceral systems.

Examination. The patient was an individual with slight pallor and a coated tongue. The heart was negative. A large cystic mass the size of a foetal head at term was felt in the mid-umbilical region. The mass was freely movable, not tender; no peristalsis was seen. A small hydrocele of the right spermatic cord was felt. The examination was otherwise negative. The blood count was normal. The X-ray examination was

said to have been negative except for some evidence of "peripyloric adhesions."

The abdominal mass had the feel of a high cyst on a long pedicle. The preoperative diagnosis was mesenteric cyst or, perhaps, a benign pancreatic cyst.

Operation. (Performed by Dr. A. A. Berg on August 13, 1923.) On opening the abdomen, a tumor was encountered in the hypogastrium. The surface of the growth resembled the cystic membrane of an ovarian tumor, greyish-white in color, opalescent, very like an amniotic membrane, enveloping the small intestine. The tumor, which stretched across the hypogastric region from right to left, was about the size of a child's head. It was impossible to deliver the tumor through the incision, possibly due to its size or possibly due to adhesions to the mesentery. There was no free peritoneal fluid. A trocar and cannula were inserted into the cystic mass in the hope of reducing its size by the evacuation of its contents, but neither fluid nor gas appeared. The trocar was immediately withdrawn.

On further exploration the mass was seen to be divided into three distinct chambers, separated one from the other. One of the subdivisions of the cystic tumor was the size of an orange, another the size of a muskmelon. The transverse colon was found bound down by adhesions to the upper abdomen. The caput coli was similarly identified; it, too, was bound down by adhesions. The nature of the mass was still not suspected.

The exploration was then continued to include the small intestine. The terminal portion of the ileum was identified as it emptied into the caput coli and was followed proximally for six inches of its course. At this point the ileum was seen to enter the mass, its mesentery no longer free. There was no sign anywhere else in the peritoneal cavity of small intestine. The remainder of the ileum and the jejunum was encapsulated in the masses, most of it lying in the hypogastric mass, the remainder in the two upper and smaller masses.

Attention was now directed to the fossa duodeno-jejunalis. The upper jejunum was free and was followed for about four inches, at which point the jejunum disappeared into one of the smaller masses. It was then apparent that only the upper four inches of jejunum and the lowermost six inches of ileum were free, the remainder of the small intestine being contained in the three encapsulated masses. There was *no evidence of any retroperitoneal herniation.*

The membrane covering the cystic masses was a distinct purplish greyish-white color, opalescent, opaque and about as thick as an amniotic membrane. It was out of the question to anastomose the upper free jejunum to the free terminal ileum, so as to relieve the intestinal obstruction. The covering membrane was therefore stripped from the underlying small intestine, the attachment of the membrane to the posterior parietes being first released.

As this was done, the small intestine unfolded itself from its cramped, constricted position. *The membrane was not adherent to the small intestine nor was it incorporated into the peritoneal covering of the ileum or the jejunum. There were no denuded or bleeding surfaces on the small intestine after the membrane had been removed.* With much care the greatest portion of the limiting membrane was removed and the confined small intestine liberated. The ileum was somewhat distended, indicating a low-grade partial obstruction. The abdominal wound was then closed.

Postoperatively for a number of days the patient continued to vomit. The stomach was lavaged repeatedly and peristalsis restored. Bowels began to move spontaneously, vomiting ceased and the patient began to gain in weight and strength and was discharged, well.

In the two and one-half years following this operation the patient had recurrent attacks of abdominal pain. Vomiting occurred at intervals of several months and lasted a day or two. He was readmitted at the end of this interval, due to the occurrence of an acute intestinal obstruction. Exploratory laparotomy revealed the lower part of the small intestine encased in a thick fibrous membrane which was adherent to the abdominal wall. A definite point of obstruction was found in the last few feet of the ileum. No evidence of the previous cyst-like membrane was found. Pathological examination of the excised scar tissue revealed chronic inflammation with calcareous degeneration. The patient was discharged, well. Up to the present date (eleven and one-half years) the patient has remained in good health without abdominal symptoms and without manifestations of obstruction. Unfortunately there is no record of a histological examination of the membrane removed. The nature of this membrane was not understood; its appearance was not that of chronic peritonitis. The cystic mass contained no fluid, and so it was not in the nature of a true cyst.

Case 2. History (Adm. 399280). (Referred by Dr. H. H. Epstein of Jamaica, L. I.)

A single man, 25 years of age, was seen for the first time on August 27, 1936. He gave a history of repeated recurrent ischiorectal abscesses for which he had been operated three times, once in 1929, once in 1934, and again in 1936. For the past two and one-half years this young man had been suffering from steady aching pains in the right lower quadrant, gradual in onset, irregular and intermittently present. Subsequently he developed a diarrhea with five to six mucoid and, at times, bloody movements a day. The diarrhea would last from one to three days, at intervals of about one week; between the episodes of diarrhea the patient was constipated. There was no history of fever and his appetite was good. There had been a loss of weight of twenty-two pounds.

The course of the disease was not continuous. He had, for instance, a remission of two months. During the remainder of the two and one-half

years the attacks of cramps and diarrhea were irregular in occurrence and in intensity.   His eating habits were regular; he had four cups of coffee a day and smoked ten to fifteen cigarettes daily.   There were no other symptoms and no previous illnesses that suggested a clue to the etiology.

Examination.   The patient was a somewhat pallid individual.   There were a few sibilant r+âles of the left apex posteriorly.   An indefinite mass could be felt in the right lower quadrant, sausage-shaped, irregular

Fig. 1. (Case 2.)   Radiograph of barium meal eight hours after eating, showing delay in the terminal loops of the ileum.

and occupying the region of the ileocecal valve.   One could not be sure whether the mass was distended cecum, inflamed granulomatous ileum, or a mesenteric mass.   The lower abdomen was sensitive, but no rebound tenderness and no abdominal wall rigidity were observed.   Examination of the region of the anus and the region of the rectum showed several postoperative scars of rectal infection with fistulization suggesting the possibility of tuberculosis, originating in a tuberculosis of the terminal

ileum and cecum; or, since we have now become accustomed to associating some anal fistulae with regional or terminal ileitis, it was considered that a non-specific granuloma of the ileum with anal fistulae was a fair presumptive diagnosis. A chest plate was taken and reported as a "healed fibroid phthisis" of the left apex. The sputum examination was negative. A barium enema taken two months before admission was negative. The terminal ileum was not visualized. Gastro-intestinal radiography, as of June 1936, was reported as showing a "fuzzy appearance" of the small intestine, incomplete filling of the ileum and jejunum with some delay in the three and six-hour observations. Radiographic diagnosis was one of diffuse ileojejunitis. A reexamination was performed on September 14, 1936 and was reported as follows:

"The stomach and duodenum are normal; motility was rapid. An observation made 2 hours p. c. showed the barium distributed from the jejunum to the terminal ileum, where it appeared clumped in coils which could not be separated. At the three-hour observation the stomach was empty, the barium was in the ileum, the ileal coils were narrowed, the terminal loops being 'bunched' and fixed in the pelvis, tender; the loops could not be separated one from the other. At the five-hour observation all the barium was in the terminal ileum; one loop of small intestine in the central abdomen was dilated and gave the appearance of persistent stasis. At the six-hour observation the barium was still in the ileum, none of it having passed into the cecum, the dilated loop in the central abdomen still being present. The appearance changed but little during the seven, eight and ten-hour observations, only a small amount of the barium passing into the cecum. No definite 'string-sign' could be seen. At the twenty-four-hour observation some of the barium had been expelled at a defecation. There is still some retained barium in the terminal ileum, the remainder of the barium filling the colon from the cecum to the descending portion. No amount of digital pressure succeeded in emptying the distal loops of ileum."

Operation. (Performed by Dr. A. A. Berg on October 12, 1936, under spinal anesthesia.) Exploration of the abdomen revealed the colon to be normal in its entirety. The terminal ileum was also normal. In the upper abdomen there was found a serous sac containing the lower part of the small intestine. The lower jejunum entered the sac from above by way of a narrow constricting band; below, the ileum escaped from the cystic mass but was seen to be again contracted somewhat lower down in the peritoneal cavity by another constricting band. The liver and spleen were normal.

Procedure. The sac was opened by sharp dissection. No fluid or gas escaped. The small bowel was freed in its entire course by the separation and removal of the sac-like membrane which confined it. The membrane was again of a greyish, opalescent appearance, being closely applied to the small intestine and tacking it down closely to the base of the mesentery

from whence the membrane sprang. As much of the membrane as could be seen was removed, other adhesions were released, the edges of the cut membrane were sutured laterally and the peritoneum was closed without further procedure. The patient made an uneventful recovery and has remained well to date.

The *pathological report* (by Dr. Paul Klemperer) named the condition cystic lymphangiectasis, a term analogous or identical with that of a cystic hygroma.

<div align="center">COMMENT</div>

These two cases seem to be almost identical in the nature of the abdominal symptoms and in the morphological findings at operation. In both cases there was a long history of abdominal pain characteristic of a low-grade partial intestinal obstruction. There was a slight progressive loss of weight without anemia. In both instances a caul-like formation of membrane covered a part of the small intestine, binding it down to the base of its mesentery. There are no congenital malformations of the peritoneum in medical literature which explain the findings. There was no evidence of a previous suppurative focus to explain a chronic peritonitis, nor was any lesion found in the viscera as a point of origin of a chronic peritonitis; neither did the membrane covering the small intestine in any way identify itself with those thickenings of the peritoneum which accompany the pseudo-cirrhosis of Pick's disease characterized by perihepatitis, perisplenitis, disturbances of hepatic circulation and the occurrence of an abundant ascites and pleuritis, (polyserositis). In these two cases the appearances of the liver and the spleen were normal, the resemblance to "iced" organs or peritonitis fibrosa being absent.

In the second case the pathology of the membrane was that of a cystic hygroma originating in the lymphatic apparatus of the mesentery, the membrane being covered by flat endothelial cells and reported by Dr. Klemperer as being typical of a cystic hygroma such as occurs in the most representative site in the clavicular regions of the neck.

Various types of mesenteric cysts have been described as occupying sites on the mesentery and on the serosa of the small intestine. These mesenteric cysts, usually small, the size of a nut or of an egg, occupy the upper abdomen and cause pressure on the small intestine. They jut into the peritoneal cavity, not into the intestinal lumen, are frequently multiple and rarely cause obstructive symptoms. They usually contain clear fluid, sometimes chyle. Chylous cysts, due to obstruction of various types in the chyle passages in the receptaculum chyli or in the thoracic duct, have also been described. Occasionally dermoid cysts have been described in the medical literature as found within the peritoneal cavity. The membranes of all these cysts are covered with endothelial cells. Most of these cysts occur in the region of the small intestine, few in the region of the

mesocolon. Baraban (1) mentions the fact that smooth muscle fibers are occasionally found in the walls of these cysts and he considers them to have originated from large lymph vessels or a large lymph sinus. Most of these lymph cysts, however, contain a chylous fluid. Occasionally the contents contain no fat but only clear watery serous fluid in which only a trace of albumin can be demonstrated. They are generally regarded as retention cysts resulting from stasis of lymph or chyle causing dilatation of the cisterna chyli or of the lymph vessels. The origin of such lymph stasis is said to be from a congenital or thrombotic narrowing of the thoracic duct or of the vasa efferentia of the lymph nodes, though the multitude of collateral lymph vessels would speak against such an origin.

Ewing (2) in his text-book entitled "Neoplastic Diseases" gives considerable attention to the subject of cystic lymphangiectiomata. In general, he describes lymphangioma cysticum as "a multilocular cystic tumor which occurs chiefly in the neck and the sacral regions. They are usually of congenital origin, exist at birth, and shortly develop into tumors of considerable size and wide extent". Retroperitoneal and mesenteric lymphangioma occur as multilocular, cavernous and cystic tumors, originating along the spinal column, ramifying into the pelvis, behind the kidney or colon, and into the mesentery or omentum. The receptaculum chyli and the thoracic duct have been found unaffected by the process in this type of lymphangioma. The walls contain connective tissue, often much smooth muscle fiber and also lymph follicles.

Sick (3) assumes that these lymphangiectatic cysts arise from misplaced and embryonal islands of connective tissue and lymph vessels.

However, the two cases just described by us do not seem to fall into the category of mesenteric cysts, since there was present no chylous fluid, nor was free fluid seen in the sac. For lack of a better comprehension it seems advantageous to fall back upon the histological report of a hygroma cysticum, a semi-solid cystic mass composed of dilated lymph spaces lined with endothelium, usually not containing fluid and occupying the sites of large lymphatic vessels. As far as we have been able to ascertain from the literature, there has been no previous description of a cystic hygroma or of a cystic lymphangiectasis of the peritoneal cavity with the clinical features of a chronic incomplete obstruction of the small intestine.

It would seem well, however, to call the attention of the medical profession, particularly of the surgeons, to the occurrence of such an unusual phenomenon as is illustrated in the two cases in our text, in the hope that a better understanding of its pathology and a clearer concept of its nature will result from observation of more and similar cases.

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THE LEWISOHN CITRATE TRANSFUSION IN THE TREAT-MENT OF ECTOPIC GESTATION

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This paper is based on 581 cases of ectopic gestation, covering the period between 1903 and 1937, treated at The Mount Sinai Hospital. It is in no way meant as a strictly statistical resumé. On the contrary, its purpose is to show to the present generation of gynecologists how much easier and less harrowing the treatment of the cataclysmic type of patients is today than it was a generation ago.

My recollection does not go back to the preoperative era when Schauta (1) wrote that the diagnosis was made mainly at post mortem, except in those cases in which encapsulation and hematocele formation developed. In those days 69 to 95 per cent of patients died of ectopic pregnancy. However, at the outset of my activities there was still an active debate going on among gynecologists as to whether or not patients in shock should be operated upon immediately. Hunter Robb (2), after cutting the ovarian arteries of normal pregnant dogs and finding that they did not die of hemorrhage, was a strong advocate of non-operation. Such debates today are, of course, of purely historical interest. At The Mount Sinai Hospital, cataclysmic patients were operated upon at once.

Upon admission, while the operating room was being prepared (and at that time this often required a full hour), the shocked patients were put in steep Trendelenburg position, and a liberal dose of morphine was injected; in bad cases, the extremities were bandaged and then, after the abdomen was opened, an infusion was given by cutting down and exposing the vein. In some ways, this era resembled the pre-anesthetic times when extreme rapidity of operation was essential and we were proud to be able to report that the entire procedure took ten, twelve or fifteen minutes in simple cases. The operating room was often a scene of confusion, as the operator had to remove the accumulated blood by dry sponging, with the help of the Trendelenburg posture. I know of two instances in which general surgeons failed to find the small rupture of an interstitial pregnancy with the abdomen full of blood, the flood of blood hiding the minute rupture which was only discovered post mortem.

Frequently our main anxiety was postponed to the postoperative period when the extreme anemia handicapped the patient in her recovery. Until approximately 1910 our sole method of helping these patients was to

continue the intravenous saline infusion, to keep them with feet elevated in bed by means of shock blocks, stimulating with hypodermics and so-called "stimulating enemata" containing caffeine, whiskey and milk.

By 1908, artery-to-vein transfusion, either by means of direct artery-to-vein suture, or the Crile or Elsberg cannula, began to be used. This procedure, however, was so time-consuming, difficult and often so un-satisfactory that it was rarely resorted to.

In the first series of 80 cases which I reported (3) covering the period from 1902 to 1908, which partly overlaps Urdan's later series and is there-fore not included in the statistics of this report, 7 were in the cataclysmic stage. Of these, 2, or 28 per cent, died of shock and anemia, which is not surprising with the methods available for relief. In this series there was active hemorrhage in 19, 3 having hemoglobin of 30 to 40 per cent, and 4, hemoglobin of 40 to 50 per cent.

In the Urdan (4) series which, in part, also includes the transfusion era, there were 14 deaths in 474 cases. Seven of these deaths were due to postoperative complications, unconnected with shock and hemorrhage. Part of these complications can be ascribed to the difficulty of the cases, 2 of which were secondary abdominal pregnancies. The causes of death not ascribable to anemia, were bronchopneumonia in 3, intestinal ob-struction in 2, eventration in one, and peritonitis in one.

Of the remaining 7 deaths, 4 occurred in the pre-transfusion era, three, twenty-four and forty-eight hours after operation, none of these patients rallying from the condition or the intervention practiced.

Two of the patients died in the early days of transfusion, one after having received 450 c. c. of blood by my "link method" (5); the other, 500 c. c. for a big secondary hemorrhage by direct artery-to-vein trans-fusion, an amount which today would be considered quite insufficient for her degree of anemia.

Dr. Robert Walter, while resident on the gynecological service, has con-tinued the statistics by looking up the ectopic gestations from 1930 to 1937, 107 cases with 3 deaths. Two of these 3 deaths can in no way be ascribed to shock and anemia. The first was due to paralytic ileus, the second was an unusually complicated abdominal pregnancy in which twins, six inches long, were found in the abdominal cavity, and where the situation of the placenta necessitated hysterectomy. The last of the deaths was one in which acute gonorrhea, syphilis, and intraligamentous rupture of an ectopic gestation produced a very confused picture. The death of this patient might possibly be ascribed to the blood loss, three transfusions, each of 500 c. c. having been given within sixty hours.

Looking over these three series, it will be noted that in the first one, from 1902 to 1908, no transfusions were available. In the series from 1903 to 1930 (474 cases) transfusion was only fully available in about two-

thirds of the cases, and twenty-one transfusions were given, 4.4 per cent for the entire series. In the last series, from 1930 to 1937, eighteen transfusions, or 13 per cent, were used.

If the mortality rate from shock and hemorrhage is scrutinized, in the first series the number of deaths was $2\frac{1}{2}$ per cent, in the second series $1\frac{1}{2}$ per cent, and in the third series .94 per cent.

It is surprising that in the early days the results were as good as they proved to be. Today the patient is safeguarded and the operator's task made lighter by many developments.

The diagnosis of ectopic gestation is one of the most difficult to make, except when the symptomatology is characteristic or when the patient is seen in the cataclysmic state due to a large intra-abdominal hemorrhage. In Urdan's series, the correct diagnosis was made in just over 58 per cent, which, in my opinion, is good. It was considered as likely, or possible, in 72 per cent. Today the pregnancy test proves of value in a number of doubtful cases. In practically every instance it will prove positive if the fetus is still alive or if the chorionic tissues are in vascular connection with the maternal blood system (7), in other words, in cases in which progression of the pregnancy may still be anticipated.

The technic of the operation has been much simplified, since today every well equipped operating room contains an available suction apparatus by means of which the first surge of blood can be readily removed when the abdomen is opened and the operative field then can be kept dry and visible.

In abdominal pregnancy where a viable placenta is encountered, the present technic has likewise reduced the risk, making it safe to merely tie off the cord and to leave in situ without drainage a placenta, the blood supply of which is not readily controllable.

But the preoperative and postoperative course of ectopic gestation has been completely changed since transfusion has become available. On our service, with only two exceptions, the Lewisohn citrate transfusion (8) has been employed, occasionally preoperatively but more often during operation, after the bleeding vessels have been secured or after the patient has been returned to the ward. The simplicity of the present day blood grouping method, the fact that the donor is no longer needed in the operating room and that a saline transfusion can be started at once while the blood is being obtained and then, without any change of instrumentarium, the citrated blood can be added to the funnel, have made the procedure successful in the hands of the youngest of our interne staff, without disturbing the operator.

It has been our practice, if the patient shows a marked reduction of hemoglobin and appears in shock, to transfuse early. The amount utilized depends on the gravity of the anemia. In the fewest instances does primary shock and bleeding require more than 500 c. c. of blood. Only where repeated concealed hemorrhages have occurred and at the time of

operation the hemoglobin is found to be as low as 30 or 35 per cent, are larger quantities of blood necessary. Then the first transfusion may be as high as 750 c. c., careful watch being kept of the response of the circulation to this amount of fluid. In a few instances repeated transfusions have been given during the early stages of convalescence if the primary transfusion has not raised the hemoglobin reading to 50 per cent. In evaluating the necessity for giving such patients additional blood the general response of the organism, rather than the hemoglobin reading alone, must be considered. Not only does a stabilization of the hemoglobin reading require the elapse of some time, but the degree of dehydration, or its opposite, due to saline infusion, must be taken into account.

Eighteen transfusions in 107 patients gave the following results:

Number of patients	Blood (c. c.)	Hemoglobin per cent
2*	750 Postoperative	42 and 51
11	500 All postoperative	31 to 75
2	450 Postoperative	50
1	350 On operating table	70
1	400 Before operation twice 500 On operating table 500 6 hours postoperative	28
1**	500 At once postoperative 500 6 hours later 500 24 hours postoperative	32

* Died 4 hours postoperatively. Twin secondary abdominal pregnancy.
** Died 60 hours postoperatively (acute gonorrhea, lues, pneumonia, intraligamentous rupture).

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ACCIDENTAL PRODUCTION OF GRAVES' DISEASE BY DEEP X-RAY THERAPY TO THE ABDOMEN (SUPRARENAL GLANDS)

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Until recently very little was known of the fundamental etiology of Graves' Disease, and even now the etiology may be said to be unknown. Of late, however, certain observations and experiments have indicated the importance of a primary adreno-gonadal insufficiency as a possible fundamental cause of Graves' disease. This has been the concept of Marine, based on experimental work done with several collaborators over a period of years, and the evidence has been reviewed by him in a paper (1) published in 1930, entitled "Remarks on the Pathogenesis of Graves' Disease." In the present report the details of two human cases are being presented, showing fully developed Graves' disease after damage, presumably to the suprarenal bodies, caused by deep X-ray therapy administered for malignant disease of the abdomen. One of these two patients was sent to Dr. Marine by the writer with the express purpose of illustrating by clinical example the conclusion which he had previously reached, partly by prolonged animal experimentation, and this is the patient to whom he refers in the paper mentioned above. As a matter of fact, Marine's experimental work in this field dates back to 1921 (2), when, in collaboration with Baumann, he demonstrated in rabbits the effect of suprarenal insufficiency in increasing the respiratory exchange. It has been difficult for clinicians, and especially for surgeons, to consider the thyroid disorder a secondary manifestation of Graves' disease, because the therapeutic results of thyroidectomy alone in Graves' disease have been so satisfactory. The thyroid gland is almost certainly the mechanism through which the metabolic disturbance in Graves' disease is effected. Thyroidectomy is still the treatment of choice for the disease, and the results of thyroidectomy, even in a general hospital, may now be made to equal those originally secured in large thyroid clinics.

The two cases about to be reported present the first observations in human beings in which the relation between X-ray therapy to the suprarenal region and Graves' disease has been clearly recognized. They afford clinical evidence of Marine's view that deficiency of some function of the suprarenal cortex plays a rôle in the etiology of Graves' disease. In the literature there have been a number of reports of the simultaneous occurrence of Graves' syndrome and Addison's disease (3, 4, 5), and of Addison's

disease following Graves' disease; also of the Addisonian syndrome follow-
ing X-ray damage to the suprarenal cortex (Goldzieher (7)); but these are
all quite different from the production of Graves' disease secondary to
injury of the suprarenal cortex without the Addisonian syndrome.

CASE REPORTS

Case 1. A physician, aged 46, was referred to the writer by Dr. H. A.
Shaw on September 21, 1929.

Family History: Careful questioning revealed no factors in the family
history predisposing to Graves' disease. There were no psychoneurotic
factors, and this in spite of rather extensive intermarriage in the family.
Of his eight brothers and sisters, no one had any thyroid abnormality.

Past History: The patient was quite certain that he was not constitu-
tionally predisposed to Graves' disease. From the age of 25 to 30, he had
been subjected to terrific stress and strain, but had experienced no symp-
toms of Graves' disease or any emotional disturbance. He stated that, if
he had had any constitutional anlage to Graves' disease, he would have
developed symptoms during those earlier years. He had suffered from
attacks of diphtheria, typhoid fever, migraine, peptic ulcer and appendi-
citis. He had always been aware of the fact that his right testicle was
undescended (cryptorchidism).

In March 1923 a large retroperitoneal growth was discovered in his
abdomen. This was considered a sarcomatous growth arising from the
undescended testicle. The tumor extended from the lower abdomen to
the umbilicus, and was accompanied by loss of weight. After six weeks of
massive X-ray therapy, the abdominal tumor temporarily disappeared.
In January 1924 he was suffering from elephantiasis of both legs, probably
due to mechanical obstruction. In May 1924 a large tumor appeared in
his epigastrium, which was again treated by deep X-ray therapy. Further
X-ray treatments were given in a prophylactic way to the spine and head.
By the late fall of 1924, after numerous X-ray treatments, the patient
noted asthenia, emaciation, hypotension (blood pressure 90 mm. of mer-
cury systolic and 60 mm. of mercury diastolic), leucopenia and anemia
(hemoglobin 45 per cent). He made a diagnosis on himself of hypo-
adrenia. In May 1925 the thyroid gland was noted to have enlarged. In
August 1925 he received further intensive X-ray treatment to the trunk
because of unexplained vomiting. He was fairly well until February 1926
when the swelling of his legs recurred.

Present Illness: In March 1926 he collapsed while at work, and was
found to have a pulse rate of 168 beats per minute. At this time his wife
noticed a definite stare of his eyes, and shortly thereafter exophthalmos
developed. The diagnosis of Graves' disease was made at that time. The
basal metabolic rate was found to be plus 56 per cent. He subsequently
developed the typical picture of severe Graves' disease with loss of weight,

diarrhea, enormous appetite, tachycardia and extreme restlessness. In February 1929 the Graves' disease was intensified by an upper respiratory infection. Bilateral corneal ulcers developed, as well as auricular fibrillation with congestive heart failure. At that time the basal metabolic rate rose to plus 76 per cent. He was given Lugol's solution and the basal metabolic rate dropped to plus 46 per cent, and then to plus 23 per cent. In April 1929 a subtotal thyroidectomy was performed. The pathologic report was as follows: "The histological picture is practically identical with that of a goitre of Graves' disease. Large parts of the gland are free from alveolar luminae. Some foetal adenomata were present." The pathologist's diagnosis was "Goitre of Graves' disease. Foetal adenoma of the thyroid."

When the writer saw this patient for the first time on September 21, 1929, he had recovered from the thyroidectomy and had resumed the practice of medicine. In July 1929 his basal metabolic rate had been −5 per cent, and he had gained considerable weight (weight, 164 lbs.).

The physical examination at this time showed that his general condition was good. His color was ruddy. There was a definite exophthalmos; Von Graefe's sign and Kocher's sign were present. A chronic hypertrophy of both tonsils was noted. There was no tremor. The surgical scar was healed. The lungs presented no abnormal physical signs. The heart was not enlarged to percussion; its rate was 60 beats per minute. The second aortic sound was accentuated. His blood pressure was 170 mm. of mercury systolic and 92 mm. of mercury diastolic. Palpation of the abdomen revealed no masses. There was diffuse pigmentation of the legs, and varicose veins. The left testicle was normal. The right testicle was undescended. The knee jerks were normal. The electrocardiogram showed a left ventricular preponderance and low T-waves. He was seen subsequently on December 29, 1930 at which time his blood pressure was 126 mm. of mercury systolic and 80 mm. diastolic, but otherwise there was no change in his condition. The exophthalmos had persisted.

Summary and Comment (Case 1). The patient in his family and previous personal history presented no factors predisposing to Graves' disease. He developed an intra-abdominal tumor (diagnosed as a sarcoma of an undescended testicle) which was treated with massive doses of X-rays intermittently from April 1923 to August 1926. By March 1926, i.e. about three years after beginning the treatment, he developed typical Graves' disease. This was relieved by thyroidectomy. The patient had become convinced that his symptoms were due to X-ray damage to the function of the suprarenal glands. Since the relief by thyroidectomy, he has remained comparatively active and well. As it is known that the adrenal cortex may be seriously damaged by deep X-ray applications, and in view of our knowledge of the effect of a deficiency of some function of the suprarenal cortex on thyroid activity, it was quite reasonable to sup-

pose that the X-ray injury to the cortex played a rôle in the etiology of his Graves' disease.

Case 2. The writer had known this patient since boyhood and believes that he had the anlage for a constitutional Graves' disease. The patient was a neuropsychiatrist, 59 years of age at the time of his death.

Family History: One maternal uncle had a goitre. On the paternal side there were no factors predisposing to thyroid disorders.

Past History: His history was suggestive of rheumatic fever before the age of 12, and that diagnosis had been made. In 1915 he had an arrhythmia, due to sino-auricular block, some nervousness, and slight enlargement of the thyroid gland. Subsequently in 1915 he suffered from an attack of catarrhal jaundice, and after recovering he was given some X-ray treatment to the thyroid.

On October 12, 1922, thirteen years before his death, a left nephrectomy for hypernephroma was performed by Dr. Herman L. Kretschmer. In the specimen at the site of the ligature of the pedicle some tumor tissue was found. He therefore received large doses of X-ray, and also radium, applied to the left side of the trunk. In 1916 he was operated upon by Dr. Phemister for acute gangrenous appendicitis. In 1928 he was subject to attacks of angina pectoris, and in that year his basal metabolic rate was plus 9 per cent. He was under the care of Dr. Milton Portis who took several electrocardiograms in 1929, which showed transitory attacks of auricular fibrillation and other disturbances of rhythm.

On November 5, 1929 he was again examined by the writer and was found to be extremely nervous, activated and had lost weight. There was no exophthalmos. Both lobes of the thyroid were enlarged, the left much more than the right. The cardiac rhythm was regular, the rate 70 beats per minute. There was a prolonged but distant diastolic murmur, and evidence of hypertrophy of the left ventricle of the heart. The spleen, liver and kidneys were not palpable. The knee jerks were present. The electrocardiogram depicted a left axis deviation, and an inverted T wave in lead 3. The blood pressure was 166 mm. of mercury systolic and 68 mm. of mercury diastolic, but he had previously had blood pressures as high as 180 mm. of mercury systolic. There was an X-ray dermatitis over the site of the nephrectomy. His basal metabolic rate was plus 25 per cent. A diagnosis of Graves' disease, secondary to X-ray damage of the adrenal cortex, was made and he was referred to Dr. Lahey of Boston for thyroidectomy. On January 25, 1930 an intrathoracic adenoma of the left lobe of the thyroid was removed. Parathyroid-like bodies were transplanted by Dr. Lahey into the right sternomastoid muscle. By the spring of 1930 his basal metabolic rate was normal. When examined in May 1930 there were no abdominal masses. The diastolic murmur was still present. An X-ray study of the lower extremities for bone metastases revealed no abnormality. He had had only one other attack of angina

pectoris. He returned to his professional work in California and reported himself in excellent condition in 1932.

Terminal Illness: His subsequent history from an entirely different angle has been published as a case record of the Massachusetts General Hospital in the New England Journal of Medicine (6). I am greatly indebted to Dr. Edward D. Churchill and to Dr. Tracy B. Mallory for permission to publish notes from their records, including the protocol of the post mortem examination. Five months prior to admission to the Massachusetts General Hospital he had low back pain; he gradually deteriorated, and was brought to Boston in a grave condition. The diagnosis considered was probable metastatic malignant disease, most likely due to a recurrence of the type of renal cell carcinoma (hypernephroma) which had been removed thirteen years previously. On the one possible chance that the diagnosis might be hyperparathyroidism, Dr. Churchill explored the neck, but no large parathyroid was found. The patient died eleven days postoperatively.

A complete necropsy was performed by Dr. Mallory on December 7, 1935, which is given here in abstract form.

Anatomical Diagnoses: Recurrent renal cell carcinoma, left, with invasion of inferior vena cava and vertebrae, and with metastases to the lungs. Pulmonary edema, bilateral. Adenocarcinoma of right kidney. Endocarditis, chronic rheumatic mitral with stenosis. Arteriosclerosis, marked coronary, slight aortic and cerebral. Prostatic hyperplasia. Operative wound: Parathyroid exploration. Operative scars: Left hemithyroidectomy; left nephrectomy. Chronic vascular nephritis.

Gross Diagnoses: Recurrent renal cell carcinoma with invasion of inferior vena cava and metastases to vertebrae, skull and lungs. Pulmonary edema, bilateral. Operative wound: Parathyroid exploration. Operative scars: Left hemi-thyroidectomy; left nephrectomy. Arteriosclerosis, marked coronary, slight aortic and cerebral. Prostatic hyperplasia. Mitral stenosis.

MICROSCOPIC ANATOMY

Kidney: "A section of the right kidney shows little glomerular damage. The capillary loops in a few glomeruli are shrunken and remain as a homogeneous mass in the center of the capsule, but only a rare glomerulus shows hyalinization. The tumor mass is found at the edge of the section of the kidney. It consists of an irregular growth of epithelial cells. They are arranged in cords, columns and tubules, and in places a definite papillary adenomatous picture. In places their formation suggests the tubular structure of the kidney. A few large cells with clear cytoplasm are found but they represent but a small part of the tumor growth.

Mitotic figures are present in small numbers only, in contrast to their

abundance in the recurrent tumor on the left. The morphologic differ-
ences between this and the recurrent tumor are so great as to produce a
definite impression that this growth represents a second primary renal
tumor rather than a metastasis from the kidney."

Tumor: "The recurrent tumor of the left kidney consists of a mass of
closely packed epithelial cells. The cells are undifferentiated, polygonal,
with clear pink cytoplasm and large deeply stained vesicular nuclei. Many
mitotic figures are found. No water clear cells are found. There is
extensive necrosis.

The metastatic lesions of the lung resemble this lesion rather than that
found on the right.

Extension of the tumor into the second lumbar vertebra is found. Here
there is extensive necrosis and the tumor mass is poorly preserved."

Adrenal gland: "Marked degenerative changes and unusually marked
and widespread vacuolization of the cells are seen throughout the section."

Dr. Mallory felt that the changes in the adrenal gland of the second
case were probably fairly recent and dependent on the terminal renal
insufficiency rather than on previous X-ray therapy. In accordance with
his suggestion to submit the section to other authorities in this field, I
sent the adrenal slide to Dr. Marine who made the following report:
"There is a marked degeneration and disappearance of the cortical cells
involving all three layers. One sees scattered islands of fairly well pre-
served cells, as if in an attempt at regeneration. The chromaffin tissue
is not recognizable. No adenomas present, nor tumor cells of any kind.
Normal gross outline of the adrenal well preserved. My impression is
that the extensive degeneration and hyaline necrosis of the cortical cells
is a result of some intoxication,—X-ray or metabolic."

Summary and Comment (Case 2). The patient had a family and previous
personal history indicating predisposition to Graves' disease. He also
had a history of rheumatic fever, arrhythmias and angina pectoris. Thir-
teen years before his death a hypernephroma was removed and he was
subjected to deep X-ray therapy to the adrenal region. He developed
frank Graves' disease which was relieved by thyroidectomy. Symptoms
of multiple bone metastases appeared, and he died after an exploratory
parathyroid operation. The histological findings of the adrenal cortex
were considered to be consistent with the theory that the previous X-ray
treatment may have damaged the cortex, and this may have been an
etiological factor in producing the Graves' syndrome.

CONCLUSION

Two clinical cases are reported which indicate that severe suprarenal
injury (deep X-ray therapy) was a causal factor in the development of
Graves' disease.

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A TYPICAL FORM OF SPLENOMEGALY IN CHILDHOOD. PHLEBOSCLEROSIS OF THE PORTAL CIRCULATION

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It is exceedingly difficult to recognize the pathogenesis of splenomegaly in adult life, but it is even more difficult in childhood because children develop hepatosplenomegaly from many and different causes much more readily than adults. Splenomegaly in infancy and childhood may be due to a great variety of causes, such as leukemia, hemolytic jaundice, Gaucher's and Niemann-Pick disease, Cooley's anemia, syphilis, tuberculosis, malaria and kala azar.

In many instances the clinical and laboratory investigations can clarify the diagnosis of the condition: in leukemia, blood examination; in the aleucemic stage of leukemia, bone marrow puncture; in hemolytic jaundice, the fragility test, the increased urobilin excretion and the signs of regeneration in the blood; in Gaucher's disease, the bone marrow puncture; in Niemann-Pick disease, the blood picture and bone marrow puncture; in Cooley's anemia, the racial and familial history, the blood picture and X-ray examination of the bones; in kala azar, the bone marrow examination, etc.

However, there remains a large group in which clinical and laboratory methods fail to clarify the issue. In recent years some light has been thrown on a small group of heretofore obscure cases presenting a very definite clinical syndrome. It was found that the enlargement of the spleen was due to splenic or portal vein obstruction.

The first cases in childhood were observed and described by Türk (1) in 1912; in the pediatric literature Kleinschmidt's (2) case appears only in 1916; Byfield (5) published a case in 1924 in the American literature, Smith and Howard (6) in 1927, and in 1929 a case was observed and diagnosed by Wilson and Lederer (7) and the writers. In 1932 we had the opportunity to observe the following case.

CASE RECORD

History (Adm. 361022). An 11 year old Porto Rican girl had been treated for pulmonary tuberculosis in Beckman Street Hospital in 1926 and two years later was treated for abdominal pain in Metropolitan Hospital. Her markedly enlarged spleen was discovered in 1926. The child fatigued easily and had felt weak since her tubercular infection. Eight days previous to admission to The Mount Sinai Hospital in 1932, sudden ab-

dominal pain recurred and the child vomited about two tablespoonsful of dark red clotted blood. The family history was negative; the father had died of pneumonia; the mother, two sisters and one brother were well. The only infectious disease in the past history was diphtheria at the age of three.

Examination. On admission the child appeared well developed, slightly undernourished, chronically ill and rather pale. There were a few ecchymotic spots over both tibiae. The tip of the spleen extended to the midline toward the right and down to the umbilicus. There was a roughened systolic murmur. The lungs were clear.

Laboratory Data. Blood count on admission was: hemoglobin, 46 per cent; red blood cells, 2,150,000; white blood cells, 2,350; polymorphonuclear neutrophiles, 63.5 per cent; monocytes, 2.5 per cent; lymphocytes, 29 per cent; eosinophils, 5 per cent; platelets, 165,000; with occasional reticulated red blood cells. Fragility test was within normal limits. Icteric index was 8. Wassermann test was negative. Urine was negative; Congo-red 10 per cent retention. Adrenalin test showed marked contraction of the spleen with increase of white blood cells from 1,950 to 6,300.

X-ray examination showed a healed tuberculous lesion in the left upper lobe. X-ray picture of the kidneys was negative.

Course. In view of the anemia, leucopenia and hematemesis, the splenic enlargement was considered to be the result of a splenic or portal vein thrombosis.

Following a transfusion twenty days after admission a splenectomy was done by Dr. Lewisohn. In the operative note there were no remarks about dilated collateral veins. The removed spleen weighed 500 grams. Pathological diagnosis was: fibrosis of the spleen with sinus hyperplasia; chronic endophlebitis of the splenic vein. After splenectomy hemoglobin rose to 64 per cent; red blood count was 4,150,000; platelets, 628,000. The patient made an uneventful recovery. There were no bleedings. Basal metabolism before splenectomy was plus 35; after splenectomy, plus 5. The child was perfectly well three and one-half years after splenectomy.

The characteristic symptoms of splenomegaly due to embarrassment of the portal circulation in any part of its course are, besides the enlargement of the spleen, moderate or marked anemia, leukopenia and repeated hematemesis. The enlargement of the spleen is frequently discovered in early childhood, as, for example, the case reported by Lederer and Wilson and observed by us at seventeen months. A second case of a one year old child was reported by Wallgren (8). The spleen increases slowly in size. The changing size of the organ is characteristic. After hematemesis the spleen becomes much smaller, but increases rapidly in size afterwards.

The anemia can be moderate. In cases with frequent hematemesis, the anemia naturally becomes increasingly marked. Frequently in marked

anemia signs of regeneration, i.e., nucleated red blood cells, are present. The leucopenia is a frequent finding, especially in the interval between the attacks of hematemesis. Posthemorrhagic leucocytosis can obscure the picture. The thrombocytes are frequently decreased and accompanied by purpuric manifestation (petechial hemorrhages on the lower extremities).

The cardinal symptom of the disease is hematemesis. The splenomegaly is observed years before bleeding occurs. The organ is provided by arterial blood. However, the thrombotic occlusion makes the outflow of the blood into the splenic or into the portal vein difficult, but the occlusion as a rule is not complete. This causes the development of collaterals. The varicose dilatation of the veins of the stomach and esophagus easily leads to rupture of the vessels and to hematemesis. The hematemesis temporarily relieves the stasis of the blood within the spleen. As mentioned previously, one of the characteristic signs of this disease is that the splenomegaly decreases after hematemesis.

Pathogenesis. Out of twenty-nine cases of the pediatric literature, two cases of Türk, one of Kleinschmidt, and one case of Smith and Howard showed umbilical infection. Bardach's (3) case, at the age of fourteen days, showed multiple abscesses of the skin. In all other cases no history of infection in the newborn period is available. One case of Wallgren and one of Wagner (9) had tuberculous histories.

Thrombosis of the splenic vein was seen in two cases (Bardach and von Crefeld) both also involving the portal vein. Phlebosclerosis of the portal vein was observed in the case of Lederer.

Gross Anatomical Features. The spleen weighed 500 grams, was rubbery in consistence and perisplenitis was present.

Histologic Studies. In early stages widening and increase of the sinuses is present with diffuse hyperplasia of the cytoplasmic reticulum. In later stages thickening of the fibrillar reticulum of the pulp and of the follicles is seen. There are no inflammatory cells present, in contrast to the findings in cirrhosis of the liver. Otherwise cirrhosis shows a similar histological change.

Diagnosis. In the differential diagnosis cirrhosis of the liver is often difficult to rule out. The liver in portal vein thrombosis is occasionally enlarged at the beginning. Ascites is present both in cirrhosis and portal thrombosis. The presence of icterus and the result of the liver function test will assist in the diagnosis of cirrhosis. It is interesting to note that, if the ascites is observed in portal thrombosis, it often disappears after hematemesis.

The differential diagnosis between isolated splenic vein and portal thrombosis is exceedingly difficult. The presence of ascites points to portal vein thrombosis. However, in the presence of a sufficiently developed hepatopetal collateral circulation ascites is often absent in portal vein oc-

clusion. For this reason a decision as to the actual site of the occlusion of the portal circulation cannot be reached in the case now presented.

Treatment. The only rational treatment of phlebosclerosis of the portal circulation is the early removal of the spleen. This operation may have a satisfactory result as long as the collateral veins are not too numerous and not dilated too much. The longer the phlebosclerosis continues, the greater is the danger that the amount of blood in the collateral circulation will increase. The burden upon the collateral circulation cannot be sufficiently relieved by splenectomy. The more or less frequent recurrence of hematemesis, in spite of splenectomy, demonstrates that the collateral circulation persists. Repeated rupture of dilated veins will ensue. It is our experience that in such cases death may follow from a fatal hemorrhage.

Early operation is, therefore, indicated with the hope of avoiding the further increase of dilatation of the veins. Early diagnosis is not only of clinical interest, but is necessary for correct treatment. The results of splenectomy in adults with obstruction in the portal circulation are less satisfactory because the operation is performed late in the disease.

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B. FRIEDLAENDER ABDOMINAL INFECTIONS DUE TO PER-
FORATIVE LESIONS OF THE INTESTINAL TRACT

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Largely because of medical tradition, a false conception concerning the rôle of B. friedlaender in infections of various parts of the body has persisted in the medical world for seventy-five years. In the minds of most physicians, and in almost all text-books on bacteriology and medicine, the organism is associated predominantly with pneumonia and other infections of the respiratory tract, whereas infections of other parts of the body are regarded as relatively less common. This point of view is emphasized by the fact that its common synonyms are "bacillus pneumoniae" and "pneumobacillus" and that even its modern scientific designation according to the Bergey bacteriological nomenclature is "Klebsiella pneumoniae."

The bacteriological experience of our hospital contradicts this tradition. Among 198 cases of infections of various parts of the body due to the B. friedlaender group of encapsulated gram negative bacilli, the organism was encountered in the respiratory tract in only 25 instances. In only 2 of these could we feel reasonably sure that we were dealing with a primary B. friedlaender pneumonia. In 7 other cases of lobar pneumonia or bronchopneumonia, B. friedlaender was encountered in the sputum or blood during life or in the lungs at necropsy in association with pneumococci or streptococci. These 7 cases were probably primary pneumococcus or streptococcus infections of the lung, in which the B. friedlaender appeared as a secondary invader either preagonally or post mortem.

The organism was also encountered in 16 other infections of the respiratory tract, of which 9 were cases of sinusitis, otitis media or mastoiditis. In some of these instances, a pneumococcus or streptococcus had been the primary infecting agent and the B. friedlaender was either a secondary mixed infection or it had been introduced as a casual contamination.

Even if we include all 25 cases as authentic examples of B. friedlaender infections of the respiratory tract, the relative infrequency contrasts sharply with the fact that the abdomen was the site of an infection with this organism in 163 of our 198 cases. Among this group of 163 cases, the most common cause of the B. friedlaender infection was found to be a perforative lesion of the appendix or the colon (61 cases). The second and third most common sites of infection were the urinary tract (50 cases) and

the biliary tract (46 cases). There were only 6 infections of the female genitalia and 10 of miscellaneous parts of the body.

Although B. friedlaender was encountered most commonly in intra-abdominal suppurations due to perforative lesions of the intestinal tract, these 61 cases do not indicate the true relative frequency of this site of infection. The number was limited by the fact that cultures were usually omitted by the surgeons when operating upon intra-abdominal suppurations.

Of the 61 cases, 53 were appendicitis abscesses. In 16, the organism was cultured from the pus in association with one or more other organisms of the intestinal flora, most frequently B. coli. The organism was also recovered from subphrenic collections of pus, peritonitis probably of appendiceal origin, peritonitis complicating an intestinal obstruction, peritonitis due to perforating carcinoma of the cecum, pelvic abscess secondary to a sigmoid diverticulitis with vesicosigmoid fistula and a perirectal abscess.

We have made no systematic attempt to determine the frequency of the encapsulated gram negative bacilli in the intestinal flora, but Dudgeon (1) has found it in the feces of 5.5 per cent of normal and abnormal individuals. Kendall (2) regards B. friedlaender as an almost constant habitant of the intestinal tract of nurslings, common in the intestinal contents of bottle-fed infants and frequently present in small numbers in the adult intestinal tract. The organism has also been isolated from the stool in some cases of enteritis (Berthelot and Bertrand (3), Jampolis, Howell, Calvin and Leventhal (4), Abel (5), Zinsser (6)).

Our observations upon the relative frequency of B. friedlaender infections of the gall-bladder and biliary passages and of the kidney and urinary passages lead us to believe that this organism frequently gains entrance from the intestinal tract into the systemic or partial circulation. Normally, it can then be excreted by the liver or kidney without giving rise to infections in the biliary or the urinary tract. However, patients in whom there is stasis to the free flow of bile or urine due to the presence of calculi, neoplasm or other mechanical factors, are more apt to develop an excretory infection of the biliary or the urinary tract. A mechanical factor of this type was found in 40 out of 46 cases of B. friedlaender infections of the biliary passages and in 44 out of 50 cases of infections of the urinary tract. Without a mechanical predisposing factor such excretory infections rarely occur.

That these infections of the normal paths of bacterial excretion are derived primarily from the intestinal tract is amply demonstrated by the frequency with which B. friedlaender was found to be associated as a mixed infection with other organisms of the intestinal flora. This was especially true of the urinary tract, in which mixed infections were found in 13 out of 50 cases. The associated organisms were B. coli, B. alkaligenes, B.

pyocyaneus, or the enterococcus. In one case the blood as well as the urine contained both B. coli and B. friedlaender.

Mixed infections were less frequent in gall-bladder and bile duct infections. They were found in one case in association with B. coli and in another with B. coli and B. proteus. This relative infrequency may have been due in part to the inhibitory effect of bile upon some of the intestinal flora.

In spite of the fact that the bacillus of friedlaender is encountered most commonly in pyogenic infections of the abdominal cavity, due to perforative lesions of the appendix and large bowel, it rarely gains entry into the blood stream from this site. We have not observed a case of bacteremia from this cause in a large experience with 16 B. friedlaender bacteremias. Of this series, 6 B. friedlaender bacteremias arose from infections of the liver and biliary tract, 6 from infections of the urinary tract, one from an acute otitis media complicated by mastoiditis and suppurative meningitis, one from a postoperative meningitis, probably due to fecal or skin contamination during convalescence from an operation for spinal cord tumor, and one from an infection of the uterus and adnexa.

In one other case the organism was recovered in a blood culture from a patient with aplastic anemia only two and a half days before death. This blood culture also contained colonies of staphylococcus albus and streptococcus alpha so that we are probably justified in concluding that the bacteremia represented a preagonal blood invasion in a patient dying slowly of a wasting and debilitating disease.

The greater frequency with which B. friedlaender is cultured from the blood or the lungs post mortem is probably due to the fact that it may enter the blood stream from the intestinal tract terminally, sometimes in company with other organisms of the intestinal flora. This may explain the error made originally by Friedlaender (7) who thought that he had discovered the cause of pneumonia when, in 1882, he found his organism in post mortem spreads made from the lungs of 8 patients who had died of pneumonia. In fact, the medical world also thought at that time that the cause of lobar pneumonia had been found, until Weichselbaum (8) described the diplococcus pneumoniae four years later.

Nevertheless, Friedlaender's bacillus continues to be called the bacillus pneumoniae or the pneumobacillus. Our experience justifies the recommendation that these names be abandoned as misleading and that the official bacteriological designation Klebsiella pneumoniae be changed to Klebsiella friedlaenderi. This review of 198 cases of B. friedlaender infection indicates that the organism is predominantly associated with abdominal infections, especially suppurations due to perforations of the appendix and colon, and next most frequently with infections of the biliary and the urinary tract. In this respect the organism conforms pathogenically with B. coli and other gram negative bacilli of the intestinal flora.

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POST TRAUMATIC SUBDURAL HYDROMA

(Subdural Accumulation of Cerebrospinal Fluid)*

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In 1924 Naffziger (1) stressed the importance of the clinical picture caused by the accumulation of cerebrospinal fluid in the subdural space following head trauma. When, in 1927, I (2) reported the details of a case history illustrative of such a condition the meagre literature on the subject was collected. Since that date the only cases listed by title are those of Petit-Dutailles and Christope (3) and J. G. Love (4). Reference to the clinical entity is, however, made by Kennedy and Wortis (5) in a recent paper on acute subdural hematomas and by Fleming (6) in a paper on the treatment of head injuries. In an article on the same subject Furlow and Sachs (7) recorded eight instances in a total of ninety-six operations for complications of head injuries. Munro (8) encountered it seven times among sixty-two subdural hematomas.

Since the publication in 1925 by Putnam and Cushing (9) of their paper on subdural hematoma, attention has been focused on that subject with the result that individual series up to sixteen cases have been reported of the chronic type of that lesion, while much larger numbers have been published of the acute variety. However, as mentioned by Elsberg in the foreword to my case report (2), and more recently stressed by Dandy and by Munro (8), the differentiation between subdural hematoma and subdural collection of cerebrospinal fluid is not always possible before operation. In fact, Munro includes his seven cases among the sixty-two hematomas he reports and considers them all part of the same process. The cerebrospinal fluid collection he considers the result of a small hemorrhage in a large amount of cerebrospinal fluid.

During a period in which twenty cases of chronic subdural hematoma were observed by me, there were four cases in addition in which the subdural collection was cerebrospinal fluid. Two of those presented a condition which would correspond to the acute hematomas, the symptoms dating from the time of the severe trauma and requiring early operation. The other two suffered a slight trauma and were not operated upon until

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* Subdural Hydroma, a term suggested by Dandy, seems an excellent one. He considers chronic subdural hydroma about as frequent as chronic subdural hematoma. Dean Lewis, Practice of Surgery (W. F. Prior Co., Inc. 1932), Vol. XII, Pp. 306-309.

many weeks later. The first case, previously published (2), will be but briefly described.

Case 1. Following a trivial injury a twenty year old man developed headache and neurological signs pointing to a left-sided lesion. At operation a subdural collection of fluid was evacuated. This constantly reaccumulated over a period of three months.

D. R. (The Mount Sinai Hospital Adm. 254497) was admitted on April 26, 1925, six weeks after a blow over the bridge of the nose received in a boxing bout. Headache began the following day and was continuous. Four days prior to admission he had a generalized convulsion and three days later he developed speech disturbances. The first physical examination disclosed speech limited to a few set phrases. There was early papilledema, a right lower facial weakness, slight loss of power in the right leg, and a Babinski response on the right. The following day there was no evidence of aphasia. During the next two weeks the papilledema progressed to four diopters, a bilateral rectus palsy appeared, the neck became rigid. Lumbar puncture on two occasions yielded xanthochromic fluid under increased pressure. A trephine exploration on May 12th, followed by a left osteoplastic flap on May 26th, was carried out by Dr. Elsberg. Operation disclosed upward of 300 c. c. of xanthochromic fluid beneath the dura crowding the brain mesially and backward (Fig. 1). The brain showed no tendency to expand after the fluid was removed. During the next two months fluid was aspirated repeatedly from beneath the dura. Two hundred cubic centimeters or more were removed at each tap. Papilledema persisted until a right subtemporal decompression was done on July 22nd, after which the eyegrounds cleared. Fluid, however, was removed up to two days prior to the patient's discharge from the hospital on August 22nd. During the four months' period more than 2300 c. c. of fluid were removed.

Comment. While this patient began to have symptoms immediately after the trauma, they were progressive and constant only for the headache and the papilledema. The other symptoms and signs such as diplopia, aphasia, loss of power and changes in the reflexes, varied from day to day. In other cases reported, as well as in those we have observed, the removal of the fluid is followed by expansion of the brain without further accumulations. In this case fluid reaccumulated, its character changed in that it became less and less yellow. To explain the reaccumulation a tear in the arachnoid must have been present and persisted. It acted in the nature of a valve like the tear in the visceral pleura in a pneumothorax. Fluid passed into the subdural space from the subarachnoid space, but could not pass the other way.

Case 2. A male, aged 25 years, was struck by a truck, with a resultant fracture of his left leg. Under observation he developed paresis of the left

arm. Trephine exploration seventeen days later disclosed accumulation of fluid beneath the dura. Death occurred.

L. H. (Hospital for Joint Diseases Adm. 55209). A twenty-five year old man was brought into the hospital September 27, 1935 immediately after
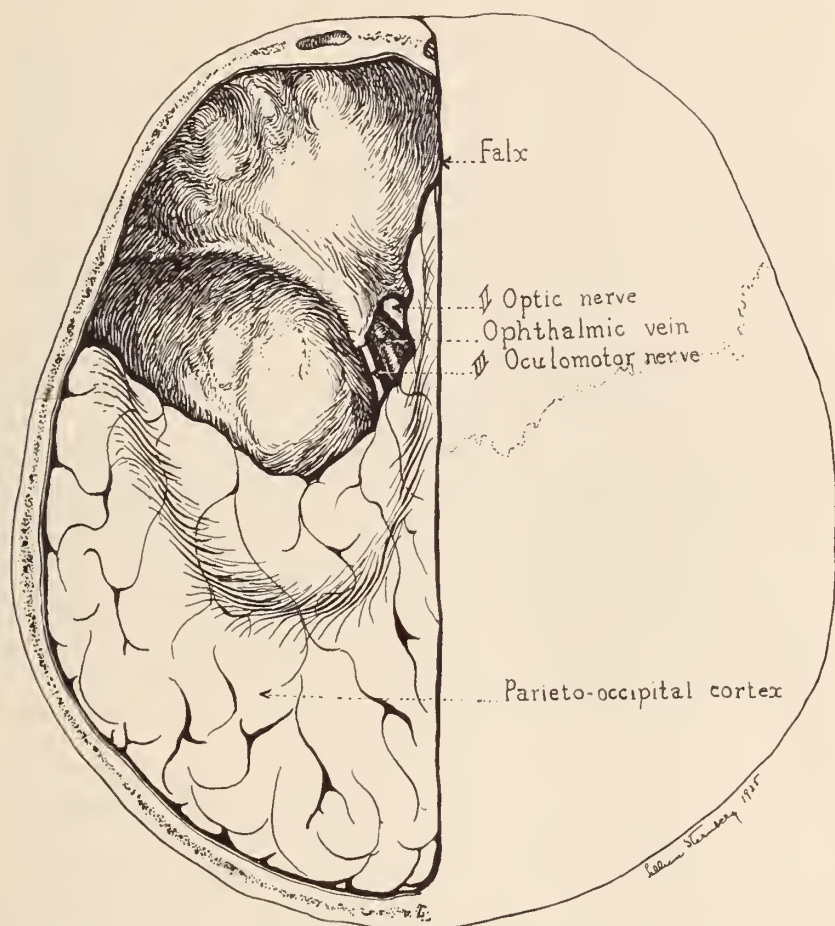
FIG. 1. Diagrammatic illustration to show the compressed brain seen at operation with the floor of the anterior and of part of the middle fossa exposed and the optic nerve, ophthalmic vein and oculomotor nerve visible. From the author's paper in Archives of Neurology and Psychiatry, November, 1927, Volume 18, Pages 709–723.

being knocked down by a truck. He had a fracture of his left leg. He was stuporous but could be aroused. There was a swelling over the left parietal region. There were no neurological signs. X-ray studies of the skull were negative. The following day a lumbar tap yielded pink fluid. During the next week his condition remained about the same. He was drowsy

but could be aroused and would cooperate. About the tenth day his temperature, which had been about 101°F., rose to 102°F. and remained between 102 and 103°F. I saw him first on the seventeenth day after the injury, at which time there was a paresis of the left arm, a weakness of the left face, and the left pupil was larger than the right. His general condition was poor. Under a diagnosis of probable left subdural hematoma, a trephine exploration over the left parietal region was carried out under local anesthesia. A gush of clear fluid followed the opening of the dura. It is estimated that at least 60 c. c. were removed. A half inch space was noted between the dura and the brain which did not pulsate. The temperature, which had been rising before operation, continued elevated and the patient died thirty-six hours later. The medical examiner reported death as due to hypostatic pneumonia. •The brain was grossly normal. There was no fracture of the skull. There was no blood beneath the dura or arachnoid.

Comment. This case represents the acute type of subdural accumulation of fluid. The onset of paresis of the arm almost a week after the trauma gave the indication for operative intervention.

As is the case in many of the subdural hematomas, there was no fracture of the bones of the cranium. However, the next case presents a combination of a depressed fracture associated with a subdural collection of fluid.

Case 3. A girl struck by an automobile sustained a fracture of the vault. Under observation she alternated between semi-stupor and maniacal outbursts. The irritable phases became more frequent. Operation disclosed a depressed fracture and a subdural accumulation of fluid with contusion of the brain. She recovered.

M. Z. (The Mount Sinai Hospital Adm. 401650). On November 24, 1936 the patient, a nine and a half year old girl, was knocked down by an automobile. She was carried to a nearby hospital in an unconscious state. When consciousness returned she was irritable and uncooperative. During her stay in this hospital she was semi-stuporous most of the time, but, when aroused, was irrational. Four days later she was transferred to The Mount Sinai Hospital. She then presented a healing laceration in the left parietal region beneath which was a hematoma. Beyond the hematoma a slight depression could be felt. There was a right central facial weakness. The deep reflexes on the right were more active than those on the left. The abdominal reflexes were present and plantar responses were normal on both sides. There was no loss of power. The fundi were normal. The left clavicle was fractured. It was impossible to be certain of speech disturbance, as no cooperation was obtained, but it was believed that an aphasia was present. The mental state varied between drowsiness and mild restlessness which seemed to come in waves. The child would awaken from sleep to sit up and shriek, and stare about without any sign of recognition of her parents. During these outbursts

no spoken word was used. A lumbar tap yielded faintly xanthochromic fluid under increased pressure which could not be accurately measured because of the struggling of the patient. Two days after admission she spoke a few words. In spite of sedatives, the periods of extreme restlessness became more frequent. On the fourth day after admission an exploratory craniotomy was performed under avertin and local anesthesia. On the left side the depressed fracture was exposed in the parietal region. Some of the fragments were elevated and some removed. The depression was very slight. When the dura was incised the brain in the region of the posterior part of the Sylvian fissure presented a contusion. Elsewhere the appearance of the brain was normal, but beneath the dura was a layer of xanthochromic fluid, which continued to well up as that in the exposed field was removed by suction. A burr hole made on the opposite side revealed nothing pathological. Improvement following operation was slow, though the extreme restlessness was not quite as marked. On the tenth postoperative day she was discharged, at which time she was cooperative and quiet. She had no neurological signs, but did have a partial aphasia which has since cleared up.

Comment. While there was no progression in the neurological signs, the increasing pressure showed itself by the increasing irritability. When the patient first came under observation periods of quiet alternated with those of restlessness in a rhythmic manner. As time went on, the restlessness dominated the picture. Not only were the outbursts more frequent, but they were more violent and prolonged. The localized contusion of the brain with its reaction held the cortex against the dura in the upper part of the exposed field. Below this there was a space between the brain and the dura occupied by the fluid which accumulated in large amounts toward the base.

The fourth case most closely corresponds to the usual picture of chronic subdural hematoma.

Case 4. Following a trivial trauma there was loss of memory and nervousness and headache with minimal neurological signs. Exploration eight weeks after the trauma revealed a bilateral subdural accumulation of fluid. Recovery resulted.

Y. G. (The Mount Sinai Hospital Adm. 400949). A housewife, 42 years of age, was admitted to the hospital on November 12, 1936. The history first obtained was that she had headache for six weeks and loss of memory and nervousness for four weeks, all of which she attributed to a gastrointestinal upset. About eight days after admission information was obtained of a slight blow to the forehead received as she leaned forward over a secretaire. A small lump resulted from the blow, but it seemed so trivial that it was not recalled at first by any member of the family. Headache dated from this injury. Loss of memory began two weeks later and was so extreme that the patient could not recall her sister's name.

The physical examination showed few objective signs. There was a
slight right central facial weakness, diminished abdominal reflexes on the
left, and a bilateral Babinski sign more constant on the right. At times
the pulse rate was as low as 68 per minute. The patient cooperated well
in her mental examination, but showed defects in retention and recall.
Memory was defective for both remote and recent events. There was no
speech difficulty (she was right-handed). Emotionally she was somewhat
unstable. Laboratory studies were not of help in reaching a diagnosis.
The only deviation from the normal was in the cerebrospinal fluid; it was
under a pressure of 180 mm. and contained 20 cells, all mononuclear in
type.

Before the history of the trauma was obtained, the diagnoses entertained
were brain tumor, unlocalized, and some type of inflammatory lesion.

Air injected in the lumbar sac for pneumograms failed to enter the ven-
tricles. When the antecedent trauma was disclosed a diagnosis of chronic
subdural hematoma was made. Under this diagnosis operation was
carried out on November 20th. Bilateral trephine explorations were made
under local anesthesia. On both sides the brain was found separated
from the dura; on the left side about 6 mm.; on the right side about 1
cm. The space was filled with clear cerebrospinal fluid which was removed
with suction.

Three days after the operation the patient was able to recall the details
of the head injury. Memory continued to improve, but up to the day of
discharge from the hospital, somewhat over three weeks after the opera-
tion, the Babinski reflexes remained positive.

The persistence of these reflexes left a feeling of uncertainty that there
might be some lesion in addition to that of subdural accumulations of
fluid.

Comment. The mental changes in this patient, shown by the tremen-
dous memory defect of which, however, she was well aware, completely
dominated the clinical picture. The improvement in this sphere was
prompt after the operation. In this respect the clinical course resembled
some chronic subdural hematomas in which the somatic signs are few and
evanescent, while the mental changes are constant.

The simplest and most ready explanation for the presence of cerebro-
spinal fluid in the subdural space in these cases is that it escaped from be-
neath the arachnoid through a tear in that membrane. This theory is
perfectly satisfactory in the acute type, the gradual accretion of fluid soon
causing sufficient pressure to demand attention within a relatively short
time. A similar condition at times follows craniotomy carried out for the
removal of a brain tumor. In these cases the flap is elevated by a collec-
tion of cerebrospinal fluid under it, which may require one or more aspira-
tions. The question arises: Does the same mechanism hold for that type

of case which presents a latent period of weeks before the symptoms force the patient to seek relief?

In chronic subdural hematomas a commonly accepted theory is the one expounded by Gardner: that the hematoma increases in bulk by dialysis through the two adjacent membranes, that is, the deep membrane of the hematoma and the arachnoid. Munro believes this may also hold for accumulations of subdural fluid if we assume some blood in the subdural space. The protein concentration in the extra arachnoid space accounts for dialysis through that membrane. We require some such explanation to account for the cure brought about by the simple procedure of removing the fluid from the subdural space, especially in the more chronic type of case. For, if the accumulation were due to a persistent tear in the arachnoid, there is no reason why it should not reaccumulate, as indeed it did in Case 1. Even in this instance the persistence of the xanthochromia suggests an additional factor other than an escape through a hole in the arachnoid. This factor was not recognized at the time of the original publication of that case.

The clinical picture of both the acute and chronic type of subdural hydroma is the same as the corresponding variety of subdural hematoma. The operative treatment is similar. The fact that a differential diagnosis cannot be made is of academic interest only. Moreover, if the theory of the evolution of the lesion, suggested by Munro, is correct, then the two conditions are but variations of one lesion. It would be well for the present, however, to consider them separately in order to gather more information and stimulate further observation of the subdural accumulations of cerebrospinal fluid.

SUMMARY

1. Four cases of subdural hydroma are reported. Two of them are of the "acute" and two of the "chronic" type.

2. The similarity to corresponding types of subdural hematomas is discussed.

3. Certain observations on the evolution of the lesion are pointed out which suggest their very close relationship to the hematoma group.

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ENDOMETRIOSIS OF THE ABDOMINAL WALL AND SCAR

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DEFINITION

Essentially endometriosis is the term applied to the occurrence and growth of endometrial-like tissue in abnormal locations. The lining of the uterine cavity is the only normal situation for endometrium. The presence of endometrial-like tissue in such sites as the uterine musculature, ovaries, round ligaments, bladder, peritoneum, rectum, etc., constitutes the abnormality. The lesion may be solitary or may involve many organs. Various names have been applied to the lesion depending on its site. The following table indicates the wide variety of terms used and the distribution of the lesion.

Name of disease	*Situation of disease*
1. Endometriosis	Uterine muscle, round ligaments, ovaries, rectum, vagina, peritoneum, bladder, rectovaginal septum, lymph nodes, urachus, laparotomy scars, umbilicus, thigh.
2. Adenomyosis	Uterine musculature, uterine fibroids
3. Fibro-adenomyosis	Uterine fibroids
Adenomyoma / Adenomyomatosis	Uterine wall
4. Endometrial cysts / Chocolate cysts	Ovaries
5. Salpingitis isthmica nodosa	Tubal angles
6. Hystero-adenoides metastatica	Lymph nodes in combination with other organ involvement

ETIOLOGY

The cause of this condition has not been, as yet, definitely determined. However, numerous hypotheses have been promulgated to account for the lesion. Up to the present the following may be accepted as explaining at least some of the cases, and it is probable that all of them play a part in the production of the condition to a greater or lesser degree.

1. *Inflammation.* It is conceivable that the irritative reaction caused by inflammatory processes may produce a lesion resembling endometriosis. Salpingitis isthmica nodosa is an example.

2. *Hormonal influences.* The reaction of the coelomic epithelium to hormonal stimulation may result in the formation of endometrial-like

structures (Lauche-Meyer). The coelomic epithelium is the embryologic structure from which the true endometrium develops.

3. *Sampson's theory.* The accidental transportation and implantation of endometrial fragments by tubal regurgitation during menstruation, following curettage, or by laparotomy, is an important etiologic factor in many cases.

4. *Metastatic implantation of endometrium* (Halban). This may occur by means of the blood or lymph stream and accounts for the occasional presence of endometrial-like tissue in distant structures, such as lymph nodes.

ANATOMICAL FEATURES

Gross. In general, the characteristic lesion, regardless of situation, consists of a more or less cystic, or solid nodule or nodules varying in size from that of a pin-head to that of an orange, and usually showing evidence of a fresh or old hemorrhage. Variation in the gross pathologic appearance depends upon the extent and location of the process. The hemorrhage associated with the lesion is due to activation of the tissue by the same hormonal factors which produce menstruation since the endometrial-like tissue responds, as does the normal endometrium.

The following descriptions represent variations in the gross appearance according to the location of the lesion in the various organs.

The *uterine wall,* the *interstitial* part of the *tube* and in *uterine fibroids*: the organ involved shows increase in size at the site of the lesion. The area is hard in consistency and not infrequently small pin-head sized or larger blebs, bluish in color, are seen on the surface. When the tubal angles are involved they become prominent and the lesion then appears as small fusiform protuberances.

The *cervix,* when involved, discloses a densely hard, almost cartilagenous lesion which may be associated with firm adhesions of the cervix to the anterior rectal wall. When the "portio" is superficially involved the lesion may be seen in the vagina as a small raised blue area not larger than a split pea, the pathognomonic "blue dome cyst."

The *ovaries,* when affected by endometriosis, display the formation of cysts, the sizes of which vary from microscopic to that of a large orange. Very rarely do they reach a larger size. The cysts are blue or brown in color and their walls are thin and so friable, due to hemorrhage and adhesions, that, on attempted removal, they almost invariably rupture, with the escape of a thick, tarry chocolate material.

Peritoneal implants may be many or few. They usually appear as tiny, raised, bluish or purplish blebs with smooth surfaces. At times only dense white puckered scars are found, as evidence of previous blebs and indicators of subperitoneal sclerosis.

Vaginal lesions, when occurring by direct extension from the cervix or

uterus, appear as bright red tissue which bleeds easily. When metastatic, bluish cysts are formed, which may vary in size from that of a pin-head to that of a pea, and also represent the typical "blue domed cyst."

The *rectum*, when infiltrated, usually is affected on its anterior and lateral walls, rarely posteriorly. The area involved becomes densely hard, even cartilaginous in consistency, but the lesion rarely penetrates the mucosa. This peculiarity must be borne in mind, in differentiating it from carcinoma. Beside the rectum, the rectovaginal septum is also concomitantly involved and may be represented by so dense a sclerotic mass that operative removal is not only inadvisable, but often technically impossible.

The *bladder* involvement manifests itself by the invasion of its wall down to the mucosa with the formation of bluish cysts, easily recognizable at cystoscopy. The presence of involvement of the umbilical region or of a postoperative scar usually is denoted by a semi-cystic mass, varying in size, that, at times, if close to the skin, has a bluish color.

On section of the involved tissue, the cut surface presents cavities, varying in size, containing a brownish, grumous fluid or a thick tarry or chocolate material. There is a tendency toward the occurrence of fibrosis in the cyst walls.

Microscopic. The characteristic lesion consists of scattered glandular structures lined by epithelium varying from low cuboidal to high columnar and resembling the glands of the endometrium. Old blood, detritus and pigment granules are usually found within the gland. A cytogenous tissue composed of masses of small round cells resembling the endometrial stroma surrounds the glands. Areas of dense connective tissue may also be present about the glands. At times glands alone are present, while at others only cytogenous tissue is found. The wall of the "chocolate" cysts may contain typical endometrial glands and a cytogenous stroma. In the large cysts the usual histologic picture may be lost, due to the pressure of the accumulated blood. The wall is a fibrous membrane containing phagocytic cells full of blood pigment, inflammatory cells, some pseudoxanthoma cells and occasional areas of cystogenous tissue with or without glands.

SYMPTOMATOLOGY

Endometriosis is a disease of the female exclusively. It occurs usually only during the active sexual life of the individual, but cases occurring after the menopause have been reported. In addition to the typical symptoms associated with a pelvic neoplasm, atypical uterine bleeding is the most frequent complaint. Dysmenorrhea also is noted, even when the lesion itself is limited to the ovaries.

Involvement of the rectum or rectovaginal septum may give rise to lower abdominal pain, backache, rectal tenesmus and spasm. Neither diarrhea, constipation or melena are common complaints. When the

bladder wall is infiltrated, vesical tenesmus, dysuria and frequency are noted, as well as occasional hematuria, especially at the menstrual period. Involvement of superficial regions like the lymph glands, vagina, umbilicus or postoperative scar may give rise to nodules which appear bluish in color and often swell and become painful at the midinterval or during the period, and subside when this phase of the cycle ends.

DIAGNOSIS

The correct diagnosis of the condition is important when the question of therapy arises. As was previously mentioned, the disease is found exclusively in females during the period of sexual activity and, only very occasionally, afterwards. The history of atypical bleeding, often associated with dysmenorrhea, in the absence of a history of previous inflammatory disease, except in cases of salpingitis isthmica nodosa, is suggestive.

Physical examination, when the uterus is involved, usually reveals a symmetrical enlargement of that organ, except when fibroids also are present and involved. In the event of ovarian involvement, a cystic adnexal mass, unilateral or bilateral, tender and fixed, is felt. There is no clinical or laboratory evidence of inflammation. The usual examination of the vagina may not infrequently reveal the presence of the pathognomonic "blue domed" cysts. Umbilical lesions and lesions in a laparotomy scar are recognized as tender bluish small cystic tumors, and the patients themselves often volunteer the information that these nodules enlarge and become painful during the menstrual period or at the midinterval. Digital rectal examination, when the rectovaginal septum is also involved, reveals infiltration of the septum and of the anterior rectal wall. The annular constriction or hard, elevated, ulcerated mass, so common in carcinoma, is not present. In addition, the proctoscopic examination will show that the mucosa is intact. Cystoscopic examination to determine the presence of the process in the bladder is only of value if the small cystic lesions can be seen under the mucosa, where they appear as bluish elevations, which may show active bleeding if the examination is made at the time of menstruation.

TREATMENT

Three methods may be employed in the treatment of endometriosis. They are:

1. Conservative operative removal of the involved tissue.
2. Radical operative removal of the pelvic organs, especially of the ovaries.
3. Radiotherapy to produce castration.

The procedure to be chosen in the individual case depends upon many factors. As can readily be understood, since the condition occurs almost

always during the child-bearing period and is never an imperative operative condition, conservatism must be the key-note. The age of the patient, as well as parity, are important. In the older woman a more radical form of therapy can be employed.

In the young woman, i.e., up to the age of thirty-five years, who desires pregnancies, a lesion involving only the uterus may be treated by curettage alone, which procedure may be of sufficient temporary value to allow for subsequent conception, before symptoms necessitating a more drastic form of therapy occur. In the event that curettage fails to relieve the condition, supravaginal hysterectomy alone should result in cure. If, however, symptoms indicating an extension of the process recur after operation, a castration dose of X-ray to the ovaries will terminate the process. In the presence of endometriosis within a fibroid, with or without involvement of the tubal angles, a supravaginal hysterectomy is indicated. Subsequent radiotherapeutic castration, if the condition recurs, may be performed.

In the younger female involvement of the ovaries calls for as conservative a procedure as is possible. If it is feasible, a conservative resection may be done. When the lesion is too extensive to permit such a procedure and the condition is unilateral, salpingo-oophorectomy on the side involved usually is sufficient. Of course, subsequent occurrence on the other side may necessitate either another laparotomy with hysterectomy and salpingo-oophorectomy or radiotherapeutic castration alone. If both ovaries are involved, with or without the uterus or other viscera, an attempt at conservative resection of one or both ovaries should always be given a trial. Should it prove unsuccessful, either a second laparotomy with removal of the ovaries and uterus or radiotherapeutic castration may be resorted to. Even when serosal implants accompany endometriosis of the ovaries, the above procedures, in the order indicated, are urged. When the ovarian involvement is so extensive that both ovaries are replaced by large "chocolate" cysts, a bilateral salpingo-oophorectomy is the procedure of choice. As a rule, it is wiser to perform a supravaginal hysterectomy at the same time, if the additional operation does not add greatly to the risk. Recently it has been suggested that temporary X-ray amenorrhea be employed as a method of treatment in young women.

In the older woman, unless the desire or need for children is great, conservatism need not be practised. Bilateral salpingo-oophorectomy alone, or combined with supravaginal hysterectomy, is the best procedure.

The presence of involvement of the rectum or bladder definitely contraindicates operative interference with these viscera. Attempts at removal of the process in these locations frequently results in the formation of fistula or recurrences. While extensive resections will cure the condition, these, because of the attendant dangers, are not advocated.

Castration, either operative or radiotherapeutic, or both will cure the most densely infiltrating visceral lesions. In the event that an absolute preoperative diagnosis of the condition is made in women over thirty-five years of age, radiotherapeutic castration is the specific remedy. Following radiotherapy, however, complete cure is delayed. Pain may persist for a long period of time and, possibly due to the subsequent scarring at the site of the lesions, an uncomfortable, prolonged post-radiation convalescence may result.

In a previous publication,* I described a young woman in whom this disease process had extended from the posterior wall of the cervix and rectovaginal septum into the vagina, presenting as a tri-lobed polypoid mass. The condition was cured only after a supravaginal hysterectomy and bilateral salpingo-oophorectomy were performed. Today we would attempt to treat this condition by the removal of the vaginal tumor and by temporary or permanent castration by X-ray.

A second unusual case is described.

ILLUSTRATIVE CASE

History. The patient was first seen on September 18, 1929. At that time she was 24 years old, married, had one child and was desirous of having more. Her chief complaint was severe right-sided, lower abdominal pain, only during her periods. The physical examination revealed only a small nodule in the right uterine horn. When seen seven months later, the mass had grown to the size of a large orange and the right ovary was also cystic and tender. A laparotomy was performed at The Mount Sinai Hospital on April 22, 1930. A large adenomyoma of the right horn and numerous small ovarian implants were found. In view of the youth of the patient and her desire for more children, a conservative resection of the tumor was performed and the right tube and ovary also removed. The pathological report (Number 4019) was adenomyoma and multiple follicular cysts of the ovary. The patient remained comfortable and her periods continued normal until seven months later, when she complained of left lower abdominal pain and also noted a small lump in the abdominal scar. The condition apparently continued unchanged for a long period of time.

Six and a half years later the patient was again seen. Again she complained of left lower abdominal pain, and a mass in the scar. She also volunteered the information that regularly between her periods (about two weeks after the onset) the abdominal scar swelled to twice its normal size and became extremely tender. Examination now revealed a large semi-cystic mass in the abdominal scar about the size of a lemon. It was not movable and seemed to extend through the thickness of the abdominal

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* Geist, S. H.: A Case of Endometriosis with Polypoid Invasion of the Vagina. J. Mt. Sinai Hosp., 1: 5, 197, 1935.

wall.   On vaginal examination the uterus seemed enlarged, fixed and there was a mass present in the left horn which was attached to, or continuous with, the abdominal tumor.   The diagnosis of a recurrent adenomyoma with secondary adenomyomatosis of the abdominal scar was made.

On April 5, 1937, a supravaginal hysterectomy with removal of the attached abdominal wall tumor and the left adnexa was performed.   It was found that the uterine mass was continuous with the abdominal wall mass.   The uterine mass had perforated the peritoneum, muscle, fascia and subcutaneous fat and was covered only by the still intact skin and scar (Fig. 1).   The extensive resection of the abdominal wall made the subsequent closure, which was like that for repair of an extensive abdominal wall hernia, difficult.

Fig. 1. Enlarged, thickened uterus, normal ovary and tube.   Springing from the left horn there is a sclerotic mass containing muscle, fibrous tissue and adenomatous areas (the small, dark areas of varying size).   The huge mass of abdominal wall tumor and skin can be seen.   The wall is replaced by sclerotic tissue and presents large cysts containing old blood and debris.

It would appear that, following the first operation, the uterus became adherent to the anterior abdominal wall and that an adenomyomatous lesion in the uterus, either overlooked at the time of the original operation or developing subsequent to it, extending along the adhesions, invaded the abdominal wall, destroying the layers as it progressed.

The patient made an uneventful recovery and to date has remained well.

COMMENT

The patient's youth and the desire for children tempered the decision at the first operation so that a conservative procedure was followed.   Today, under the same circumstances, a temporary X-ray amenorrhea would

have been attempted after the diagnosis was made by laparotomy, or even after the conservative myomectomy. Whether permanent castration would have resulted in a cure instead of the second extensive operation cannot be stated, but, in view of the technical difficulties of the operation, it might be worth while attempting X-ray castration, should a similar case present itself. Should it fail, operative intervention could always be resorted to.

THE TECHNIQUE OF PARATHYROIDECTOMY IN THE TREATMENT OF RAYNAUD'S DISEASE AND SCLERODERMA

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In 1935, Bernheim and I published a preliminary report describing our experiences with six cases of Raynaud's disease and scleroderma that were subjected to parathyroidectomy. Since then eight other patients have been accorded the same treatment. A careful analysis of the late end-results is now being made and will form the basis of another communication to be published later.

It may not be amiss to review briefly the reasons, some of which are, to be sure, theoretical, which pointed to the rationale of this procedure. It has been known for a long time that the main function of the parathyroid glands is to control calcium and phosphorus metabolism. It is also well known that the bones are the main storehouse of calcium and phosphorus, being composed generally of a complex calcium salt containing calcium phosphate and carbonate ions.

The source of calcium and phosphorus is through absorption from the gastro-intestinal tract. The amounts absorbed depend on: (1) the diet; (2) the acidity of the gastro-intestinal tract; (3) the digestion of fats; and (4) the supply of vitamin D. Of these four factors, I should say that the diet and vitamin content are the most important. If any factor is at fault, absorption of calcium and phosphorus from the gastro-intestinal tract is interfered with and a negative calcium balance results. The most common examples of such disturbances are represented by rickets and osteomalacia.

Through the activity of the parathyroids, there is maintained a constant blood serum level of 9.5 to 10.5 mgm. of calcium per 100 c. c., and 3 to 4 mgm. of phosphorus. Calcium and phosphorus are deposited in the bone trabeculae through the action of the enzyme, phosphatase. However, once calcium and phosphorus leave the bones, they are not utilized again and redeposited, but are excreted. There is, therefore, no reversible internal circulation of calcium, so to speak. Calcium and phosphorus are excreted through the intestinal tract and the kidneys. If increased excretion takes place, as in disturbances of the parathyroids, a negative balance results, which, if it persists, leads to generalized decalcification due to the withdrawal of calcium and phosphorus from the bones. The first change noted is a rise in excretion of phosphorus in the urine and a fall in the inorganic phosphorus in the blood. Inasmuch as calcium is released

with the phosphorus, a marked increase in this substance is noted in both the urine and blood.

The most important variety of hyperparathyroidism is found in von Recklinghausen's disease or generalized osteitis fibrosis cystica. Two laboratory findings pathognomonic of this disease are invariably present, namely, an increased serum calcium and a decreased serum phosphorus. In addition, the blood phosphatase is markedly increased. The bony changes are noted first in the flat bones and later in the long bones. Usually, a parathyroid adenoma is the basis for the clinical manifestations and operative removal of such a tumor generally results in marked amelioration, if not cure, of the condition. The disease may or may not be associated with renal calculi.

There is another variety of hyperparathyroidism which was described by Albright, Aub and Bauer about two years ago. This disease is characterized by recurring nephrolithiasis and is due to diffuse hyperplasia of the parathyroid glands. Three such patients were operated upon by Churchill who found enormous enlargement of the parathyroids. Subtotal removal of the involved glands was followed by marked improvement in the urinary symptoms.

It has been maintained that one should never entertain a diagnosis of hyperparathyroidism unless there is found an elevated serum calcium and a decreased serum phosphorus. My experience with the fourteen cases mentioned above leads me to question the necessity of postulating these requirements. It is known that there are two, and possibly more, varieties of calcium in the body, the diffusible and the non-diffusible. It is possible that one of these forms may be increased, yet the total serum calcium figures may appear normal. In certain allergic diseases it has been demonstrated that the diffusible calcium is greatly increased, yet the total figures are within normal limits. Whether this is due to a hyperparathyroidism or to a disturbed function of the parathyroids is not known.

In my experience, most patients suffering from Raynaud's disease sooner or later develop changes in the skin which come under the classification of scleroderma. This is usually evident in the fingers and hands. I believe that the underlying cause for the development of the sclerodermatous process is essentially the same as that associated with Raynaud's disease in its primary phases, that is, vasospasm; in scleroderma, there is vasospasm of the capillaries of the skin and adjacent subcutaneous tissues. The fact that sclerodermic changes are more evident in the skin of exposed parts of the body, such as the fingers, hands, forearms, and face, suggests that cold produces reflex stimuli which accentuate an already existent spasm. There is evidence to indicate that sclerodermatous changes develop in those parts of the body where the superficial capillaries run in a horizontal direction to the skin surface. What the significance of this anatomical difference is, I am unable to say. In any event, it seems fair

to assume that the subsequent skin thickening seen in scleroderma is due to a slow interference of blood supply resulting in the deposition of scar tissue with a large collagen component. As far as our experience goes up to the present time, I would venture the opinion that Raynaud's disease and scleroderma possess the same causative mechanism and may be discussed together.

As a result of observations which cover a number of years, Bernheim and I formed the opinion that disturbances in calcium metabolism are factors in the development of Raynaud's disease and other vasospastic conditions. Calcium deficiency in the diet, common in adults, and producing a negative calcium balance, may cause, in certain individuals, an abnormal predisposition to vasospasm. We suggested in our original paper that, inasmuch as calcium affects the permeability of every cell in the body, the results of insufficient calcium intake may be exceedingly varied. We feel that the constitutional factor is of great importance in determining the reaction of different individuals to disturbances of calcium metabolism and to the development of subsequent clinical manifestations. The constitutional factor may be considered to depend upon a local inferiority which renders tissues more susceptible to damage, such as that produced by diminished blood supply through vasospasm.

To understand the rationale for parathyroidectomy in these conditions, one must begin with the important assumption that one of the functions of the parathyroid glands is to maintain a constant serum calcium level of about 10 to 10.5 mm. per 100 c. c. With long deficiency in calcium intake the stores of body calcium become exhausted, and the parathyroid glands become hyperplastic, apparently because of their increased physiological activity in withdrawing calcium from depleted bones, and possibly also from other tissues. This, then, may be regarded as a work hypertrophy of the parathyroid glands. The constitutional factor becomes a part of the picture, and eventually various clinical symptoms are manifested which bring the patient to the physician. Whether the form of calcium drawn from the bones is a different variety from that supplied through an adequate diet is still a matter of conjecture.

If such patients are given an adequate calcium regimen, many of them will respond favorably; that is, there will be a marked amelioration of symptoms which have been due primarily to vasospasm. This has been our experience in many cases of Raynaud's disease, thrombo-angiitis obliterans, and arteriosclerosis. It is our conception that in such cases, following adequate treatment with calcium, the parathyroids are relieved of their extra work of drawing calcium from the bone reserve, and may soon return to a normal physiological state. However, in certain instances, improvement does not take place in spite of prolonged treatment. We feel that in these patients a change of a more or less permanent nature has taken place in the parathyroids, resulting in hyperplasia or disturbed func-

tion, and that in such instances removal of two or more parathyroid bodies is indicated.

In none of the cases that has been subjected to operation has a hypercalcemia existed. The blood findings in these cases are not comparable to those found in cases of true hyperparathyroidism, such as osteitis fibrosa cystica. Therefore, the indication for parathyroidectomy does not depend upon the finding of hypercalcemia.
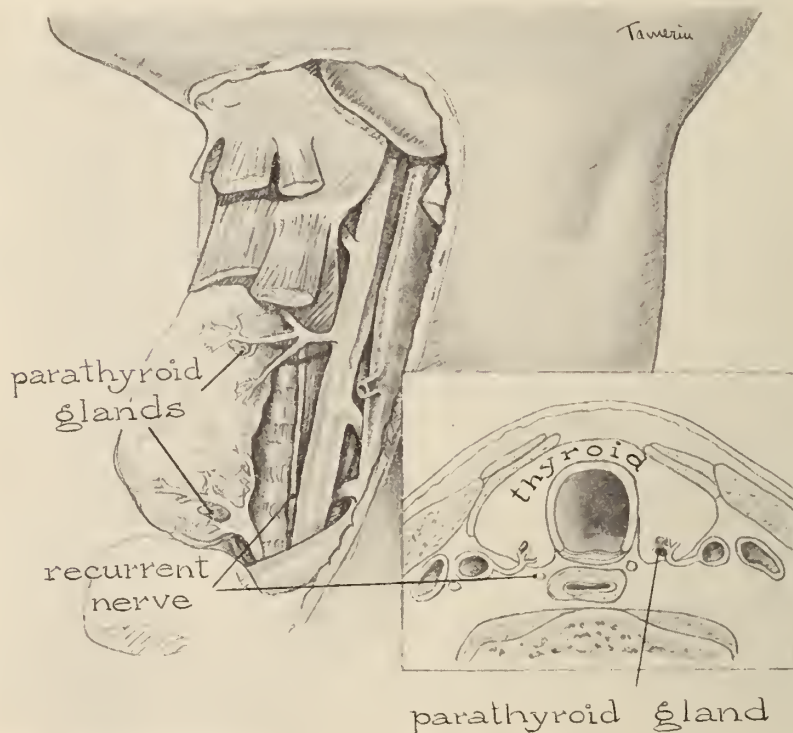
Fig. 1. Drawing of a neck dissection to show the relationship of the thyroid gland, parathyroid bodies, superior and inferior thyroid vessels, trachea, and recurrent laryngeal nerve.

The late results in the fourteen patients already mentioned will be reported at a future date. I would like, at this time, to discuss some of the technical details in the operative procedure. The preoperative conditioning of the patient is of considerable importance, to prevent postoperative development of symptoms of tetany. It consists of the administration of a high calcium-high vitamin diet for one or two weeks and of parathormone for three or four days before operation. It may be necessary to supplement the dietary calcium by oral administration of calcium lactate or

by hypodermic administration of calcium gluconate to establish a reserve of calcium in the body before proceeding with the operation of parathyroidectomy.

Surgical Technique. Careful attention to the details of the operative procedure will aid the surgeon to identify the parathyroid glands with greater ease. These include free exposure, meticulous hemostasis, careful atraumatic dissection, the use of small sharp instruments, a good light, an
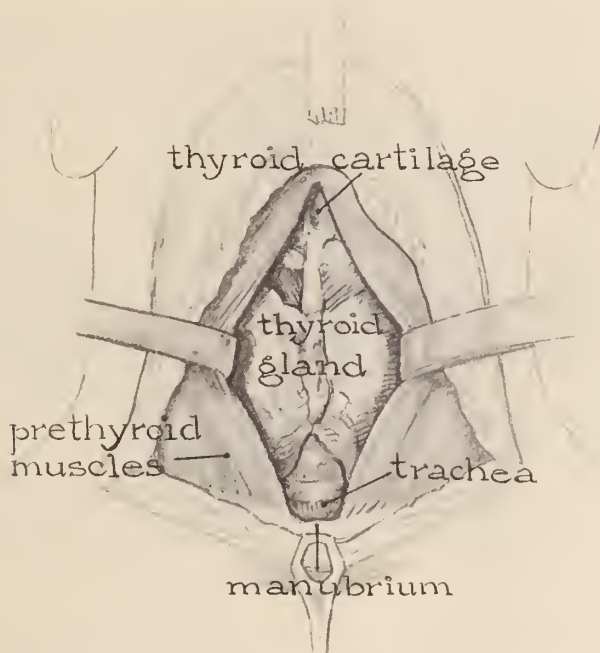
Fig. 2. Operative procedure for parathyroidectomy. The depressor muscles have been separated in the midline and retracted laterally. It is important to free the muscles from the underlying structures from the thyroid cartilage down to the suprasternal notch. If this is done it is unnecessary to divide the prethyroid musculature.

appreciation of the differences in color between the thyroid, fatty tissue and the parathyroids, and a thorough knowledge of the usual positions of the parathyroids and their anatomical variants.

Using the usual thyroidectomy incision, upper and lower skin flaps are reflected. The depressor muscles are separated through a vertical midline incision and retracted laterally (Fig. 2). I have not found it necessary to divide the depressor muscles transversely in order to obtain proper exposure, unless there is a concomitant enlargement of the thyroid. It is im-

portant to free the muscles from the underlying thyroid gland as far down as the suprasternal notch in order to insure clear visualization of the inferior thyroid vessels. Exposure of the right side is undertaken first. The right lobe of the thyroid is grasped and retracted gently toward the midline. The middle thyroid vein is doubly ligated and divided (Fig. 3). The entire lobe is now freed from the surrounding areolar tissue extending from the superior pole down to the lowest extremity of the gland. Further traction of the lobe across the midline exposes its posterior surface and also the
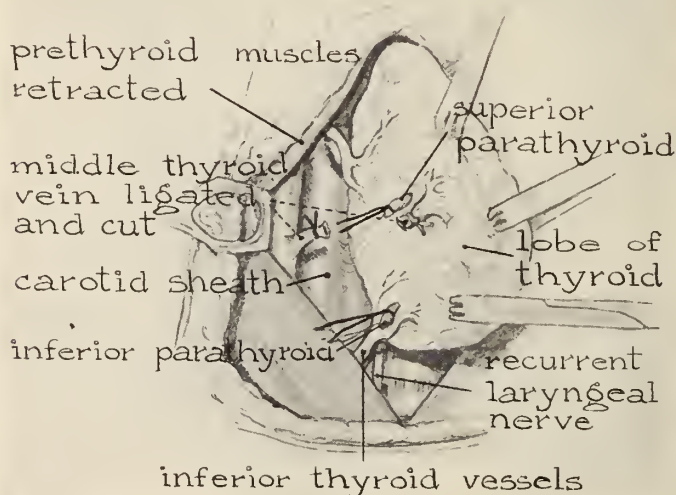
Fig. 3. Exposure of the postero-external surface of the thyroid lobe. The middle thyroid vein has been ligated and divided. The superior parathyroid body is usually found opposite the cricoid cartilage about an inch above the entrance of the inferior thyroid vessels into the gland. The inferior parathyroid body is usually located at the point of entrance of the inferior thyroid vessels. The close approximation of the carotid sheath and the recurrent laryngeal nerve to the field of operative dissection should be noted. The silk suture placed through each parathyroid body for identification purposes is indicated.

tracheo-esophageal groove. This entire region is now carefully inspected. It is important to avoid infiltration of the tissues with blood and this may be done by meticulous hemostasis as one proceeds with the dissection. The parathyroid glands are flat, oval bodies, 3 to 7 mm. by 2 to 5 mm. in size and of a peculiar tan-brown color. This color is the clue to their identity. It is quite different from the yellow of fat and the reddish-brown of the thyroid gland. In my experience, the most common site for the superior parathyroid is on the posterior surface of the thyroid gland

just external to the tracheo-esophageal groove about one inch above the entrance of the inferior thyroid vessels into the thyroid and approximately at the level of the inferior border of the cricoid cartilage. The usual location of the inferior gland is between the inferior thyroid artery and vein just before these vessels enter the thyroid gland. There may be considerable variation both as to their number and position. The location of the parathyroids in the fourteen cases that were operated upon is indicated in an accompanying drawing (Fig. 4). In only one instance was a parathyroid body found embedded in the substance of the thyroid.
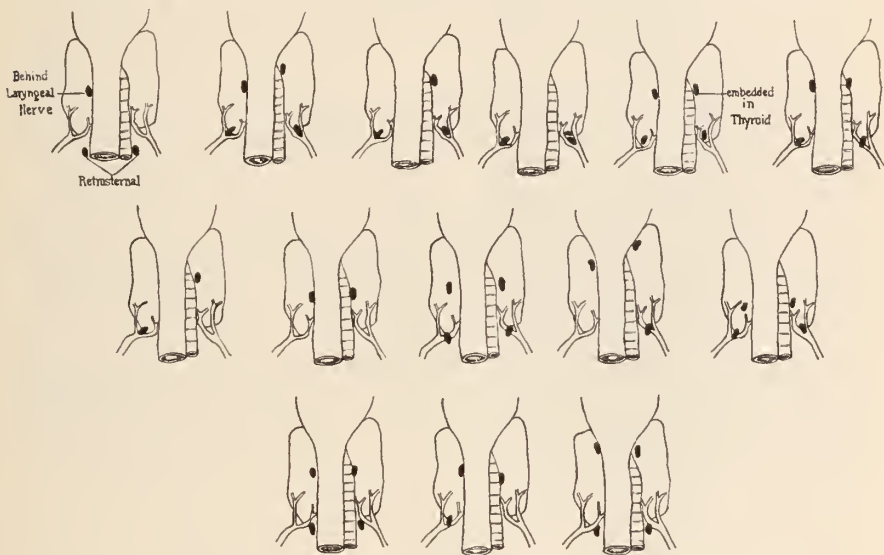
Fig. 4. Schematic drawings to indicate the position of the parathyroid bodies in each of the fourteen cases that were subjected to operation. Each drawing represents a posterior view of the esophagus and trachea and the thyroid lobes. The inferior thyroid vessels have been inserted in order to more clearly visualize the location of the inferior parathyroid body. In only one instance was a parathyroid gland found embedded in the substance of the thyroid beneath its capsule.

Every effort should be made to isolate all four parathyroids (there are usually four) before removal of any one. As each gland is isolated, a stitch of very fine black silk is passed through its tip for identification purposes. When removal of one or more glands is decided upon, its vascular pedicle should be ligated before excision. This will obviate a troublesome ooze that may occur. In the treatment of scleroderma and Raynaud's disease, I have, of late, removed two glands and performed subtotal resection of a third, when able to identify all four glands. If three glands are found, I remove two of them. Not infrequently, in order to aid in the search for the inferior glands, ligation and division of the inferior thyroid vessels becomes necessary. Although the older anatomy books indicate

that the parathyroid bodies derive their blood supply from the inferior thyroid arteries, the surgeon need have no fear of necrosis of these glands, should division of the vessels become necessary. More recent anatomical studies indicate that an anastomotic arch is made by the union of a branch from the superior thyroid artery and another from the inferior vessel and that the blood supply of the parathyroids is derived from small twigs arising from this arch. If the inferior thyroid artery is ligated, the blood supply will be derived from the superior vessels. I emphasize this point because recently Leriche, in an article in *Surgery* (1:1, 1937) implied that ligation of the inferior thyroid vessels accomplished the same result as parathyroidectomy. It seems to me that such an inference is wholly unwarranted.

After identification of the parathyroids on the right side, the thyroid lobe is replaced in its original position, following which the left side is similarly explored. More often than not, the parathyroid bodies on this side will be found to occupy almost identical positions. In order to make the identification of the glands doubly certain, a frozen section of a small piece may be made at the operating table. After the desired number of glands have been removed, the thyroid lobes are replaced in their beds and the wound is closed without drainage.

Postoperatively, parathormone is given twice daily in thirty unit doses for five or six days. The high calcium-high vitamin diet is continued indefinitely. In the fourteen cases already referred to, there have been no deaths or complications.

RENAL HYPOPLASIA AND APLASTIC KIDNEY

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The importance of recognizing renal hypoplasia and aplasia becomes evident when a study is made of fatalities which have resulted because these anomalies were not diagnosed preoperatively. A number of cases have been reported in which death from anuria ensued at intervals varying from a few days to several years, as a result of a hypoplastic kidney failing to develop sufficient reserve power to compensate for the loss of the opposite kidney. There still appears to be confusion concerning the anomalies of renal development, and for the sake of clarity we have adopted the following definitions. In hypoplasia we are dealing with a small kidney which, despite its diminutive size, may be normal anatomically, histologically and functionally. In renal aplasia there is no demonstrable organ present, only a small mass of fibrous tissue, or strands of degenerated embryonic tubules and glomeruli. There is often a lower segment of the ureter present, which may be dilated (case 5) and may or may not be connected with the remains of nephrogenic tissue. This aplastic organ has, of course, no function, although in most instances two ureteral orifices are present in the bladder. Renal agenesis signifies a congenital absence of the kidney and ureter. As a rule, there is but one ureteral orifice present in the bladder, although cases of congenital single kidney with the presence of a ureteral orifice and ureter on the side of the absent kidney have been reported. Associated rather frequently with this anomaly, are anomalies of the genital tract.

The above anomalies of the kidney represent failure of proper development during embryonic life, and must be differentiated from secondary atrophy of the kidney due to organic disease. Renal hypoplasia is found in about one in a thousand cases at post mortem examination. Whereas the normal kidney weighs about 150 to 175 grams, the hypoplastic organ is a third to a sixth of the normal size, weighing 20 to 40 grams, and rarely exceeding 4 cm. in length. On cross section the hypoplastic kidney presents the same histological structure as the normal. According to Eisendrath (1) the pelvis of the hypoplastic kidney may show the persistence of the infantile type, as seen in children, having a relatively large pelvis compared to the size of the kidney, with the minor calices arising directly from the pelvis; or the pelvis may have but one or two calices. The pelvis may be rudimentary with comparatively small calices, or there may be a

complete absence of the pelvis, the ureter apparently ending directly in the renal parenchyma. Ubelhor (2) has suggested a division of hypoplasia into two groups. 1. True hypoplasia in which the kidney is very small, but with normal parenchyma. In this group the excretion of dye and urea concentration does not differ from the opposite normal kidney. 2. Dysplasias in which there are all degrees of variation from the normal parenchyma, with correspondingly poor function, to absence of function.

Clinical Recognition of Hypoplastic Kidney. Unless there are evidences of infection a hypoplastic kidney is generally overlooked, because of the absence of clinical symptoms. The following diagnostic procedures are of aid in the diagnosis of this condition. 1. Ordinary radiography, or the flat film of the urinary organs. In general, the absence of a renal shadow on a film, should not be construed as evidence of absence of a kidney. In case 3 there was a definite shadow of a diminutive kidney on one side, with the outline of a normal kidney on the opposite side; in fact, a tentative diagnosis of hypoplasia was made from the flat film.

Excretory urography, if the function is not impaired, may yield valuable information in outlining a tiny kidney. Even if the function is impaired to the extent that the pelvis and calices are not outlined, the renal shadow itself may be intensified by the dye.

Retrograde pyelography yields more valuable information by outlining the pelvis and calices. Although there is no pyelogram which one may say is characteristic of hypoplasia, the pelvis is generally moderately dilated, usually funnel shaped, with diminutive calices showing no deformity. There may be only one or two calices arising from a small pelvis.

Cystoscopy yields but little data, as both ureteral orifices are generally present. In regard to functional tests, if there is a sufficient amount of renal parenchyma present, the excretion of indigo carmine and urea may be normal. Eisendrath has pointed out that "these are the cases which have led to the belief in the past, before the more or less routine use of pyelography, that the hypoplastic kidney possessed sufficient reserve power to compensate for diseased conditions on removal of the opposite one." Quite a number of cases have been reported where there was apparently normal urine, good urea concentration and prompt elimination of dyes, and yet the kidney at operation or autopsy proved to be a rudimentary organ.

The following cases of hypoplasia and aplasia demonstrate the importance of making a preoperative diagnosis of the presence of one of the above anomalies, before undertaking any surgical procedure on the opposite kidney.

CASE 1. STONE IN HYPOPLASTIC MISPLACED KIDNEY

History (Adm. 279644). The patient was a male, 40 years of age, who for the last year had had right-sided colics which had gradually become

more frequent. There had been no hematuria, and no temperature. The
X-ray examination of the genito-urinary tract showed a shadow just above
the posterior superior spine on the right side. The shadow was semilunar
in shape, and lay transversely along its axis. The patient's voided urine
was perfectly clear.

Examination. On admission to The Mount Sinai Hospital, X-ray stud-
ies of the genito-urinary tract showed the right kidney to be low, part of
it being in the false pelvis, and there was a stone apparently in this kidney

Fig. 1. (Case 1.) Calculus in right misplaced hypoplastic kidney

near the crest of the ileum. On pyelography, the kidney was found partly
in the pelvis, its upper pole extending a little above the crest of the ilium.
The calices were dilated and blunt, and two of the calices pointed towards
the spine, whereas the lowest calyx pointed in the opposite direction (Fig.
1). Pyelograms of the opposite kidney showed slight abnormalities, but
the kidney was placed normally and the pelvis was apparently bifid
(Fig. 2). Cystoscopy showed diminished excretion of indigo carmine
from the right kidney.

Cystoscopic examination showed that the function of the right kidney was diminished, and microscopic examination of urine obtained from that side showed some pus cells.

Operation. (by Dr. Beer: May 27, 1927). With the diagnosis of a stone in a non-rotated kidney, the right kidney was exposed through a very low incision starting in the lumbar region and coming down into the right iliac fossa, and, as the kidney was converted into a hydronephrotic sac, it was removed. The organ was found deformed and hypoplastic,

Fig. 2. (Case 1.) Pyelogram of hypoplastic kidney

and about one-half the size of a normal kidney. The pelvis presented anteriorly, and the kidney itself was held close to the midline and in the false pelvis by at least three groups of veins and arteries which entered the kidney on its mesial and anterior surfaces. In addition, one large vein ran across the lateral convexity, over the upper pole; and posteriorly a small vein entered. All of these vessels had to be tied separately, and then the ureter was ligated and the specimen removed. The kidney was about $2\frac{3}{4}$ by $1\frac{1}{4}$ inches, having a fair residual of the healthy parenchyma surrounding the dilated pelvis and calices.

The ureter, as will be seen in Figure 3, entered the anterior surface near the lower pole and divided into three branches—two wide lateral branches, and a superior branch which became a calyx at the upper pole.   In the upper pole, this extra calyx was divided into two small lateral branches. This created practically a condition without any definite intrarenal pelvis,

FIG. 3. (Case 1.)   Injected hypoplastic kidney after removal

all the branches being evident external to the kidney parenchyma except the terminal short piece.   The stone was found stuck firmly within the first lateral branch of the pelvis, near the lower pole, in the external part of the kidney.   After a mild wound infection the patient made an uneventful recovery.

CASE 2. HYPOPLASTIC KIDNEY—URETERAL CALCULUS ON OPPOSITE SIDE

History (G. L., Adm. 390742). A young man, 25 years of age, was admitted to The Mount Sinai Hospital in February, 1936. He gave a history of attacks of left lumbar colic with nausea and hematuria.

Examination. X-ray examination demonstrated a stone in the lower end of the left ureter. An intravenous urogram showed a moderate left hydronephrosis, with no visualization of the right kidney.

FIG. 4. (Case 2.) Pyelogram of hypoplastic kidney

Course. Cystoscopy was performed; the right ureter was catheterized, and pale watery urine was obtained with no indigo carmine excretion. The left ureter was catheterized to the pelvis, and clear urine was obtained with strong indigo carmine. A pyelogram of the right kidney was taken; only 2 c. c. could be injected. A tiny irregular pelvis was outlined, showing no calices (Fig. 4). A diagnosis was made of hypoplastic kidney, with a calculus in the ureter of the opposite kidney. The stone could not be dis-

lodged by cystoscopic treatments, so on February 13th it was removed through an anterior ureterotomy incision. The patient made an uneventful recovery. Intravenous urograms taken in May 1936 and January 1937 again failed to visualize the right hypoplastic kidney.

CASE 3. HYPOPLASTIC KIDNEY—URETERAL CALCULUS ON OPPOSITE SIDE

History (J. S., Adm. 404386). A male, 41 years of age, was admitted to the hospital in February, 1937, complaining of pain in the left lumbar

Fig. 5. (Case 3.) Opposite slightly dilated kidney with obstruction in ureter

region of three weeks' duration. The patient had a pulmonary tuberculosis of many years' duration, and was refused insurance 18 years ago because of albuminuria. At the onset of his present illness he had hematuria, dysuria and frequency. His general condition was fair. Blood pressure was 120 systolic and 80 diastolic. Genitalia revealed an underdeveloped penis and testes, with an atrophic prostate.

Examination. On admission, the urine was clear with a one plus albumen. Blood urea was 71 mgm. per cent. Flat film of the urinary tract showed clearly a diminutive right kidney shadow, with a normal left kidney. Intravenous urography showed poor visualization of both kidneys.

Course. During cystoscopy the right ureter was catheterized and clear urine was obtained, with no indigo carmine excretion. Urea was 0.35 mgm. per cent. The left ureter was obstructed at 17 cm. This obstruc-

FIG. 6. (Case 3.) Hypolastic kidney

tion was finally passed and 20 c. c. retention of urine was found in this pelvis, also with no indigo carmine excretion. Concentration test of urine showed fixation between 1010 and 1011. The phenolphthalein test showed 5 per cent excretion in four hours. Pyelograms (retrograde) of both kidneys, done in two stages, showed a typical hypoplastic right kidney. The left kidney was hydronephrotic with a block in the ureter at the level of the third lumbar vertebra (Figs. 5 and 6). A tentative diagnosis of a left

ureteral calculus was made.   Due to the fact that the patient's blood urea rose to 95 mgm. per cent, it was decided not to pass wax bougies to determine the presence of a left ureteral calculus.   The high nitrogen retention in this case can possibly be explained on the basis of an interstitial nephritis of the left kidney.

CASE 4.   RENAL APLASIA

History (Adm. 312832).   A male, 30 years of age, complained of right lumbar pain, non-radiating, for the past nine months.   There had been no urinary symptoms.

Examination.   The urine was cloudy, contained a heavy trace of albumin and a moderate number of pus cells.   A flat plate of the urinary tract was negative for calculus.   Cystoscopy showed an absence of the right ureteral orifice.   The left ureter was catheterized and clear urine with strong indigo carmine was obtained.   Intravenous urography showed no visualization of the right kidney.   The left kidney was hydronephrotic and the ureter was considerably dilated.   Exploratory operation failed to reveal a right kidney.   Instead, a peculiar cord-like formation resembling the rete testis was found adherent to the peritoneum.   There was no evidence of a ureter.   Histological examination of a specimen removed was reported, "Groups of convoluted tubules probably remnants of Wolffian duct or body."   The patient made an uninterrupted recovery and has been well ever since (seven years).   In addition to the renal aplasia, this patient had an undescended testicle on the same side as the kidney defect.

CASE 5.   RENAL APLASIA

History (Adm. 402198).   A male 38 years of age was admitted to the hospital because of attacks of painless hematuria.

Examination.   Findings were essentially negative.   The urine was cloudy and contained considerable pus and red blood cells.   A flat film of the urinary tract showed a large dendritic calculus filling the right kidney.   Blood chemistry was normal.   Intravenous urography failed to visualize the left kidney, whereas the right kidney was seen to be moderately hydronephrotic.

Course.   Cystoscopy revealed that the right ureteral orifice was normal. The ureter was catheterized and cloudy urine obtained with a fair excretion of indigo carmine.   In the region of the left ureteral orifice there was a bulging into the bladder about the size of a walnut, resembling an ureterocele with a tiny orifice through the entire length of which a catheter was passed.   An X-ray examination showed the catheter curled up in the lower end of the ureter.   No urine or indigo carmine were obtained from this side.   The catheter was injected with hippuran, outlining what appeared to be a hydroureter (Fig. 7).   A cystogram showed no reflux.   Under the impression that we were dealing with an ureter-hydronephrosis a left

lumbar exploratory operation was performed.   There was no kidney to be
seen, only a few buds of degenerated fibrous tissue.   The ureter was then
exposed and opened and a catheter passed down into the bladder.   Above
the incision in the ureter the lumen was completely occluded, the ureter
becoming a mere fibrous band dividing into three strands which were at-
tached to the fibrous remains of the kidney.   After removing a segment of
ureter, the lumbar incision was closed in layer suture with drainage.

FIG. 7. (Case 5.)   Right renal calculus.   Left hydro-ureter with renal aplasia

CASE 6.   HYPOPLASTIC RIGHT KIDNEY

History.   A male child, six years of age, was admitted to the hospital
in July 1929, because of joint pains and pyrexia of four weeks' duration.

Examination.   A blood culture was positive showing a non-hemolytic
streptococcus.   The child was cachectic and presented the appearance of
a sepsis with diffuse petechiae, a systolic heart murmur and a palpable
spleen.   The urine showed pus cells, granular casts and albumin; white

blood cells numbered 32,900 with 87 per cent polynuclears. The child ceased a week after admission.

Post Mortem Examination. There were evidences of a sepsis. The right kidney was absent. There was a renal rest attached to the upper portion of the right ureter, which extended to the bifurcation of the aorta. The renal body was bean-shaped; no opening of the ureter could be found in the bladder.

Microscopic examination showed the renal rest to be composed of glomeruli, tubules and fibrous tissue, with nodules of cartilage present. The ureter was divided by fibrous tissue into several compartments. The left kidney weighed 200 gm., appeared swollen, and was the seat of multiple infarcts. The adrenals showed no anomaly.

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REMINISCENCES OF THE HISTORY OF BLOOD TRANS-
FUSION

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This article is not history but rather a body of informal recollections bearing on the local history of blood transfusion. The author has a special interest in modern transfusion because he was present at its birth and has watched it grow into vigorous usefulness. This explains the personal tone of the article which the author hopes will be pleasing to Dr. Lewisohn, in whose honor it is written. Lewisohn's important work in introducing the citrate method of transfusion led to the choice of subject.

In 1901 Karl Landsteiner announced the discovery of isoagglutination and the blood groups, in a modest short paper for which, thirty years later, he received the Nobel prize in medicine (1). It is sometimes stated that Shattock independently made the same discovery, but anyone who reads his paper will see that his observations had nothing to do with the subject (2).

For a number of years no one paid much attention to Landsteiner's work. A few additional details about the blood groups were worked out, chiefly by Landsteiner's assistants. Jansky, in 1907, wrote an article (3) in Hungarian in which he attempted to correlate the groups with disease, and gave them numbers from one to four instead of the letters originally suggested by Landsteiner. All this seemed to have little connection with blood transfusion, although Landsteiner in his original article in 1901 suggested that the groups might be important for transfusion.

The rebirth of transfusion began with the classic experiments of Carrel (4), in 1906, on arterial anastomosis. After he had perfected his technic on dogs, Carrel performed a human transfusion which caused a great sensation. He transfused blood from the father, a well known New York surgeon, into the veins of the newborn child, saving the life of the child, who was suffering from hemorrhagic disease of the newborn. It turned out later that Carrel's technic was far too delicate for most surgeons to master, but at the time his work was most important because it brought the possibility of direct vascular anastomosis before the public.

My own interest in blood transfusion developed from Carrel's work and began in the following manner. In 1906, when I was senior interne in surgery at the German (now the Lenox Hill) Hospital, I had the kind of inspiration which comes to many a young interne. I said to myself, "Why

not reverse the principle of the Murphy button and use for arterial anastomosis a ring which will fit around the blood vessel in such a way as to apply the intima of one vessel to the intima of the other?" At some personal expense, which at the time seemed to me enormous, I had a jeweller make me a set of rings of different sizes. The engineer of the hospital made for me a clamp with which to hold the rings. With the aid of other internes I succeeded in performing a number of successful end-to-end anastomoses of the severed carotid arteries of dogs. These experiments were performed with the greatest secrecy (and difficulty) in the dead-house because at that time most hospitals had no facilities for animal experimentation. I was so full of enthusiasm at the success of the arterial anastomoses that I called on Simon Flexner, head of the, then new, Rockefeller Institute, and asked for a position with him, so that I could continue to work on the subject. He told me he already had one man, Carrel, working on vascular surgery, and that was enough.

When, in 1907, George Crile (5) announced that he had successfully performed a number of human transfusions, I was terribly downcast to find that the idea for the intima-cuffing ring was not new with me at all. Crile used such a ring for his transfusions, having borrowed it from Payr, who, with the aid of such rings, had performed a number of successful arterial anastomoses on dogs, in 1900. Payr, in turn, had gotten the idea from Quierolo who had proposed it in 1895.

After more than two centuries of attempted transfusions, most of which were technical failures, it was really Crile's work which again drew attention to direct transfusion. Crile's ring technic, cumbersome as it seems to us now, was easy as compared with Carrel's suture method and led many surgeons to try transfusion.

When I heard of Crile's transfusions, having already a set of silver arterial rings, I at once petitioned my attending surgeons (I was by this time house surgeon) for permission to do direct transfusions on suitable cases. Dr. Torek, then an associate visiting surgeon, helped me with the transfusions; his gentleness and calm helped to neutralize my nervous excitement. At that time I heard of the existence of blood isoagglutinins from the late Richard Weil and made my first visit to the library of the Academy of Medicine to look into the subject.

I did not realize that I had been the first to apply Landsteiner's discovery for determination of compatibility in an actual transfusion, and when, in 1908, I published an article on the arterial anastomoses and the blood transfusions (6) I merely mentioned that such tests had been done on my patients, and ventured the prophecy that they would be important for the future of blood transfusion.

After my internship was completed, I received the appointment as George Blumenthal, Jr. fellow in pathology at The Mount Sinai Hospital (this was the first of a long series of fellowships in pathology at the hos-

pital). The surgeons at Mount Sinai were already experimenting with blood transfusion. Charles Elsberg devised a rather elaborate modification of the Crile ring; Leo Buerger evolved a simpler one. As I was in the laboratory I offered to do compatibility tests, but many of the surgeons did not accept the offer. They felt that, since Crile had done a large series of transfusions without tests (and with only a few cases of hemolysis and no deaths), they ought to be free from interference by the laboratory men. It took about five years of campaigning, experimenting, and a few accidents to convince the medical public that blood tests before transfusion were essential. There is no doubt that, had tests not been introduced, the modern revival of transfusion would have subsided as did so many earlier attempts, because of the fear of terrible and unpredictable accidents. Why accidents did not regularly occur when incompatible bloods were transfused was a subject that puzzled me much at the time and to which I returned later.

In 1908 professional donors were unknown and when transfusion was proposed all possible members of the patient's family were tested. This led me to the observation that brothers and sisters were very frequently in the same blood group. I examined five full families and reached the conclusion that beyond a doubt the blood groups were inherited and followed Mendel's law. However, I encountered several inconsistencies, due to making the wrong assumption that the blood group itself was the unit character (gene). I did not realize the importance of the observations and, as my year of fellowship was nearly over, I hurriedly published a bare statement that the blood groups were inherited according to the Mendelian Law. This appeared as an incidental paragraph in an article (7) on the technic of transfusion tests written with A. A. Epstein who had proposed to me the use of Wright's opsonic pipette technic. Subsequently von Dungern and Hirschfeld in Heidelberg examined a large number of families and were easily led to the correct assumption that the agglutinogens, and not the groups, were the real unit characters in heredity (8).

Since then a vast literature has grown up concerning the heredity of the blood groups and, though the theory has been changed by the statistical studies of Bernstein, the essential facts of the dominant inheritance of the agglutinogens are so well established that the blood group tests are now accepted by the courts in cases of disputed paternity.

During the year 1910 there also appeared in the Johns Hopkins Hospital Bulletin Moss' important article on blood groups (9). Although Hektoen's article had appeared three years earlier, it was Moss who popularized the idea of blood groups with the American public. Unfortunately, Moss numbered the groups in a different order from that of Jansky (who had been followed by Hektoen and myself) and for a number of years there was much confusion due to the use of the two different numbering systems by different hospitals. After the World War a committee appointed by

the National Research Council tried to straighten the matter out by dropping numbers altogether and substituting the symbols 0 (zero), A, B, AB as the names of the four groups (10), (thus naming each group for its agglutinogens in Landsteiner's original scheme). This is now universally used in the scientific literature but the habit of using numbers still persists in medical conversation and laboratory reports. The really important contribution of Moss, however, was in pointing out that isohemolysis followed exactly the same rules and ran exactly parallel to isoagglutination, except that in many humans the hemolysin was undeveloped. It was this that made it possible to do the clinical test merely by agglutination or by determining the groups, instead of by doing the laborious hemolysis tests. It was Minot who first pointed out the simple method of assigning the proper group to any human red blood cells if one had a sample of serum of Group A (Group II) and Group B (Group III). For some years then, following the suggestion of Brem of San Francisco, it was thought sufficient to determine the group of patient and donor. But later, after Guthrie and Huck at Johns Hopkins Hospital had drawn attention to the so-called "subgroups", there was a general return to the earlier method of doing an additional test (usually called the "cross test") of the patient's serum with the prospective donor's cells.

While abroad (in 1909–1910) I made a short visit to Vienna and called on Landsteiner, but he was so excited about his recent discovery of the transmissibility of poliomyelitis, that he spent the whole time of the visit in showing me sections of monkey spinal cords, and I never got a chance to tell him of my interest in his blood groups.

When I came back to New York I took up in earnest the problem of why accidents only occasionally occurred when incompatible blood groups were transfused. Quantitative studies showed that when a relatively small volume of blood having agglutinative serum was mixed with an excess of a blood having susceptible red cells, little or no agglutination or hemolysis could be detected. The small amount of antibody was distributed over so large a number of cells that the individual red cell was too feebly sensitized to produce any effect. On the other hand, when a small volume of susceptible cells was mixed with a large bulk of blood having agglutinative or hemolytic plasma, each cell received a large amount of antibody and agglutination or hemolysis occurred, though the agglutinated clumps were small on account of the mechanical interference of the excess of unagglutinated cells. In actual transfusion the amount of blood transfused—generally 500 c. c.—is small as compared with the patient's blood volume, which is 5000 to 8000 c. c. for an average adult. Hence, I argued that it would be safe to use as donor a person whose serum agglutinated the patient's red cells, but that it might be dangerous to use one whose red cells were susceptible to the patient's serum. This immediately led to the use of Group O (I Jansky, IV Moss), whose red cells are inagglutinable

by the serum of any of the groups, as "universal group" donors in emer-
gencies: and during the World War, which began only three years after
my publication (11), thousands of such transfusions were done with suc-
cess.

Beside this work two series of animal experiments and a parallel series
of clinical observations were carried out. These were full of extraordi-
narily interesting details. In the first series agglutinative and hemolytic
transfusions were carried out in dogs (12), in the second in cats (13), in
both of which species of animals occasional, but not grouped, incompati-
bilities of this kind were found to occur. All the experiments fully con-
firmed the conclusions drawn from a detailed study of one hundred twenty-
eight human transfusions (14) (the first of its kind) that hemolysis was far
more dangerous than agglutination, but that, if agglutination was avoided,
hemolysis would also be avoided. It was also found that agglutination
of the donor's cells by the patient's serum was more important to avoid
than the reverse. In both animals and man, when the recipient's serum
had either agglutinins or hemolysins for the donor's cells, phagocytosis of
red cells by leucocytes was observed in the circulating blood after the
transfusion. Hemoglobinuria was only noted when hemolysis was in-
tense; when it was of lesser grade jaundice only appeared. As a result of
the clinical investigation it was felt that hemolytic accidents could be
definitely avoided by preliminary tests, as the only three untoward acci-
dents in the one hundred twenty-eight cases occurred in cases in which
they could have been predicted.

During 1913 also the technic of transfusion was enormously simplified
by the introduction of the multiple syringe method by Edward Lindeman
(15), then an interne at Bellevue. (It was really a revival of the Ziemssen
method of 1892). Until then the direct artery-to-vein anastomosis was
the best method available but was often very difficult or even unsuccessful.
And, what was almost as bad, one never knew how much blood one had
transfused at any moment, or when to stop (unless the donor collapsed).
(I remember one such collapse in which the donor almost died—and the
surgeon needed to be revived). The only guide one had was repeated
hemoglobin estimation of the patient, for which the transfusion would be
stopped every few minutes by pressure on the donor's artery. Dr. Libman
and I worked out a simple formula by which one could calculate how much
blood, transfused, would produce a given change in hemoglobin percent-
age (16). This formula, though no longer needed for the same purpose,
is still useful if one wishes to calculate beforehand how much rise in hemo-
globin one may expect from a given transfusion. If this calculation were
made, physicians could avoid the disappointment which they often ex-
press at the small rise, perhaps 3 to 5 per cent in hemoglobin, after what
seems like a large transfusion in a patient whose hemoglobin at the start
was, perhaps, 60 per cent.

Lindeman made such a success with his method that he became the first transfusion specialist. He ended a short, but brilliant career a few years later by drowning while swimming in the surf at night during a session of the American Medical Association at Atlantic City.

In 1914 Moss attempted to reintroduce the transfusion of defibrinated blood. This had had a long and interesting history dating back to Bischof in 1835. It had finally been given up due to numerous fatalities which were attributed to intravascular coagulation (from fibrin ferment) but which, on retrospect, were probably chiefly due to incompatibilities. In 1915 Dr. Libman and I published the first careful clinical analysis of a large series of over two hundred transfusions (17). Among the interesting observations was one whose significance has become much clearer as progress has been made in recent years in the study of pernicious anemia. Certain symptoms, such as the glossitis and the spinal cord symptoms, were found to be independent of the anemia, since they were not relieved when the anemia was temporarily abolished by transfusions. This paper was supplemented by further observations in 1917 (18).

The year 1915 was notable for advances in the technic of transferring blood from person to person. Lester Unger, then an interne at The Mount Sinai Hospital, devised his stop-cock apparatus (19) which offered many advantages over the Lindeman method. It was mechanically so perfect that it has never been improved on by any of the numerous stop-cock apparatuses offered to the public since. I well remember assisting Unger in his first experimental transfusions on dogs. Unger, like Lindeman, became a transfusion specialist. Elsberg made the clever suggestion to chill the syringe with an ether spray so as to delay coagulation.

Kimpton and Brown in the same year introduced their paraffin tube method which, though successful in their hands, offers so many technical difficulties that it has been little used outside of the place of its origin.

But the most important transfusion advance of 1915 was the introduction, simultaneously and independently by several different workers in different lands, of sodium citrate as an anticoagulant. Within the span of a few weeks appeared publications by L. Agote (20) from Buenos Aires and by Richard Lewisohn (21) from The Mount Sinai Hospital. Hustin (22) in Brussels and Weil (23) in New York also made trials with sodium citrate but in the former case the technic was inappropriate; in the latter the dose chosen was so large that for an ordinary sized transfusion it might have been fatal. Lewisohn worked out the upper and lower limits of dosage so carefully and his technic was so simple that it has hardly been changed to this day. As a result he generally is given most of the credit for having introduced the now almost universally used citrate method of transfusion.

In the history of science it is surprising how often this phenomenon of simultaneous independent discovery occurs. Only rarely is progress due

to some solitary genius far ahead of his times. Commonly when the ground has been prepared by previous workers and the time is ripe, the idea which leads to the next step in advance occurs almost simultaneously to several minds. That is why priority controversies are so frequent.

Other anticoagulants (such as hirudin) had been tried before and have been tried since (e.g. heparin of Howell) but sodium citrate possesses such advantages of simplicity, cheapness and safety that it has held the field.

During the years following the introduction of the citrate method a great controversy raged as to its alleged disadvantages, and particularly as to whether the post-transfusion chills which formerly occurred in a certain proportion of cases following all methods of transfusion, were more frequent after one method than after another. The situation was only cleared up in the years immediately following 1913, when Florence B. Siebert (24) discovered fever-producing substances in some samples of distilled water. It gradually became evident that the chills which unaccountably used to occur not only after blood transfusion but even after ordinary saline infusions, were due to extraneous contamination with foreign proteins or bacterial products. By scrupulous elimination of every possible contaminant, chills after intravenous injections are avoidable. In 1931 there was established in The Mount Sinai Hospital a special department (on the tenth floor of the Semi-Private Pavilion) with Miss Koch in charge, where all intravenous apparatus and solutions are cleaned and prepared.

Lewisohn and Rosenthal (25) published in 1933 an article giving details of this preparation, in which they could triumphantly point to the virtual abolition of chills after transfusion. Simple as the details of preparation are, they are of extreme importance. Such a centralized system as Mount Sinai has, is now established in many, but unfortunately not all, hospitals. Only last year I visited a large hospital in a neighboring city, where a member of the staff told me that severe chills after venous infusions, as well as after transfusions, were very usual and were regarded as unavoidable.

Today transfusion has become so safe and so easy to do that it is seldom omitted in any case in which it may be of benefit. Indeed the chief problem it presents is the finding of the large sums of money needed for the professional donors who now provide most of the blood.

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THE SIMULTANEOUS ASSOCIATION OF HIATUS HERNIA AND CORONARY DISEASE

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Ever since von Bergmann (1) called attention to the simulation of the anginal syndrome by a hiatus hernia we have been interested in the demonstration of such herniae in suspect cases. We agree with von Bergmann that such herniae are quite common. In the past four years we have found in The Mount Sinai Hospital twenty-one cases of hiatus hernia. The age of the patients varied between 39 and 72. In only three instances did the symptoms resemble in any way those of coronary disease. By this we mean that the main complaint was precordial or retromanubrial pain. In none was the typical radiation present, or the response of the pain to exertion or emotion.

In those instances in which the symptoms resembled those of the anginal syndrome, especially if the electrocardiagraphic changes were not characteristic, the natural inclination was to suspect the hernia as the instigating lesion. This conclusion was unquestionably valid in some cases; I recently reported such an instance (2). The following case, however, is reported to prove that true coronary disease may occasionally be associated with genuine hiatus hernia.

History. L. L. male, aged 51 years, was first seen by me on September 25, 1930. He complained of a progressive gain in weight in the past few years. Aside from a moderate weakness, he felt well.

Examination. The heart outlines were normal, the sounds were normal and the blood pressure was 124 systolic and 84 diastolic. The urine was normal. His weight was 180 pounds. In November 1931, he complained of precordial pain on walking and when excited. An examination at that time showed no new findings. The electrocardiogram, aside from a left ventricular preponderance, was normal. The blood pressure at this time was 120 systolic and 80 diastolic. He was advised to stop smoking and to reduce his weight. For a while his precordial distress was relieved but for the next few years, despite an appreciable loss of weight (over 20 pounds) and the cessation of smoking, the pain continued as a constant complaint. The pain was never severe, always transient and never possessed the characteristic radiation. Repeated electrocardiographs showed no change. The pain was rather capricious in onset and did not always follow exertion. He remained active and travelled extensively. His blood pressure on

repeated examinations varied little, ranging between 120 systolic and 75 diastolic. Fluoroscopy showed a slight bulge of the aorta, commensurate with his age, but no enlargement of any of the chambers. The heart sounds were normal. On November 1, 1936, he returned from a trip abroad, still complaining of the precordial pain. Examination again

Fig. 1. Radiogram showing hiatus hernia. This picture was taken in the Trendelenburg position.

showed no change and, in view of the clinical atypicism, he was referred to Dr. Asher Winkelstein, who found a fairly large hiatus hernia (Fig. 1). He presented no clinical evidences of gastric disorder. Despite this report, the patient was advised not to relax in his precautions. On November 4th he was found dead in his bath tub.

COMMENT

There is no question but that this patient had true coronary disease, even though clinically the symptoms were by no means characteristic and the electrocardiogram was quite normal for his age. The conclusion is inevitable that, given a patient in the declining years suffering from precordial pain, more or less related to exertion or emotion, even in the absence of the characteristic radiation and a normal electrocardiogram, the diagnosis of coronary disease is still the most probable. Hiatus hernia is only one of many extracardial disorders that may simulate coronary disease, and even though it is demonstrated in a suspected instance of coronary disease, it is not justifiable to conclude that it is the cause of all the clinical phenomena. Indeed, in our collected series of twenty-one cases, there were six in which the hiatus hernia was apparently an accidental finding. In two there were no symptoms, in three gall-bladder disease was found, and in one a carcinoma of the esophagus was demonstrated. It would prove useful to examine by X-ray a series of perfectly normal adults for hiatus hernia; the probability is strong that we would find hiatus hernia in a small percentage.

SUMMARY

A case is reported of associated hiatus hernia and true coronary disease. The mere finding of a hiatus hernia does not necessarily exclude the possibility that part or the entire clinical phenomena may be due to an associated lesion. Hiatus hernia is not infrequently a symptomless malady.

I am deeply indebted to Dr. Herman Zazeela for much assistance in the pursuit of this study.

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OPERATION AND THE CARDIAC PATIENT

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Operative intervention in a patient whose heart is diseased calls for an evaluation of the added risks that the cardiac condition introduces into the surgical procedure. Misjudgment results when heart disease is regarded as a unitary disorder. The heart is affected by a variety of diseases and reacts to the morbid processes differently at different periods of their evolution. Accuracy of appraisal is reached with the recognition that there is no one single form of heart disease, but that there are heart diseases, as well as hearts, with different degrees of functional capacity.

Cardiac disease hardly increases the operative mortality in patients who, while subject to either chronic rheumatic valvular disease, uncomplicated essential hypertension or heart disease, due either to hyperthyroidism or to some congenital defects, give no history or evidence of heart failure. For patients in this group the criteria for anesthesia and operation are practically the same as those for normal individuals. The operative mortality hardly exceeds that of normal individuals (1). A patient of this type may be subjected to an emergency operation without fear, and also to operations of choice, such as herniorrhaphies and cholecystectomies. There is much to be said for operating early while the heart is still well compensated. To delay until the condition requires surgery may necessitate operation at a time when the heart has begun to fail. In these patients there is no need for the preoperative or postoperative administration of digitalis. Fluids can be given freely both by mouth and intravenously.

Patients with coronary artery sclerosis and with syphilis of the aorta and the aortic valves are less favorable subjects for surgery. A recent study revealed an unexpected operative mortality of 8 per cent (1) in such instances. All but urgent operations should be avoided. The expectancy of life of these patients is short, and the need for operation must be balanced against the prognosis of the heart condition. If operation becomes necessary, a short anesthesia, speedy operation, minimum trauma and bleeding must be assured. In these patients an unforseen coronary thrombosis may develop at any time, even as late as several weeks after the operation. It is difficult to prove that the operation itself is the cause of such a complication, but the frequency of this association makes a causal connection probable. Patients with these forms of heart disease

are subject to sudden death, due presumably to ventricular fibrillation. This seems to occur more frequently when there is a preexisting extrasystolic irregularity. To such patients it may be wise to give 3 grains of quinidine sulphate three or four times a day for several weeks.

For patients with congestive heart failure operation is hazardous and should be resorted to only as a life-saving measure. These patients show an unexpected mortality of 17 per cent. Here is need for a surgeon of real virtuosity. There is little time for preoperative preparation of the patient. The most important measure is the speedy administration of full doses of digitalis. If the patient has had no previous medication with digitalis he may be given 4 cat units of an appropriate preparation intravenously and at the same time 4 cat units by mouth. Further dosage must be determined by the response of the heart, but, as a rule, it is quite safe and even desirable to give 12 to 15 units in the first twenty-four to forty-eight hours. The maintenance dose is from 2 to 3 units a day. If there is much venous congestion, a phlebotomy of 300 to 500 c. c. may be helpful. In these patients the administration of fluids intravenously may place too great a strain on the heart and may even precipitate an attack of pulmonary edema. This happens more often with the transfusion of blood than with the infusion of saline. When it becomes necessary to administer fluids intravenously or to give a transfusion, the fluid should be given slowly by the drip method and the patient should be kept under constant observation. Of the supplementary cardiac stimulants, caffeine sodium benzoate—$7\frac{1}{2}$ grains given every three to four hours is best. Restlessness should be combatted with morphine and appropriate sedatives. In the presence of much dyspnea and cyanosis oxygen quiets the patient and eases the work of the heart.

The presence of auricular fibrillation, as such, does not materially add to the operative risk, provided the heart rate is kept under control. Enough digitalis must be given to maintain the ventricular rate, as counted with the aid of a stethoscope, between 70 and 80 beats a minute. Measurement of the pulse rate at the wrist is inaccurate, because of the common presence of a pulse deficit. Auricular fibrillation, as a rule, develops in the late stages of heart disease, so that it occurs in the more badly damaged hearts, except in patients with hyperthyroidism.

When circulatory embarrassment is induced or exaggerated by a condition amenable to surgical treatment operation is imperative. It offers the only chance of relieving the heart of its extra burden and of restoring compensation. The most common condition of this sort is hyperthyroidism, which has either directly led to the heart disease or has aggravated some form of preexisting heart disease. Congestive heart failure is rather uncommon and is seen only in cases that persist over many years. Indeed, it occurs almost exclusively in patients who have coexistent organic heart disease.

The presence of a cardiac complication, whether it be simple enlargement, auricular fibrillation or congestive heart failure, is an indication for early operation. Only by such a radical measure can one hope to avert further cardiac damage and to restore normal cardiac function. The indication becomes all the more urgent when there is an organic heart lesion, such as valvular disease or coronary artery disease complicating the functional circulatory disturbance caused by the hyperthyroidism. Whereas the heart that is otherwise sound will carry the stress of Graves' disease fairly well for years before becoming insufficient, the heart already damaged gives way. Hyperthyroidism increases the work of the heart in much the same manner as does physical exertion. Just as one would not allow a patient with a crippled heart to engage in frequent or continuous physical exercise, so in hyperthyroidism one must relieve the heart of its additional work as quickly as possible. Only operation will accomplish this expeditiously and thoroughly. In skillful hands the operative mortality is not great. Lahey (2) reports a 3.6 per cent mortality in operations on 138 patients with serious cardiac complications, of whom 110 had congestive heart failure. Of 101 patients who were traced, 95 were returned to full activity, 19 had persistent auricular fibrillation and 6 were still disabled.

Preoperative preparation of the patient with compound tincture of iodine is carried out, as with all patients with hyperthyroidism. In the presence of auricular fibrillation or of heart failure, full doses of digitalis should be given and the fluid intake should be limited. These patients usually tolerate large doses of digitalis without the appearance of toxic symptoms. Operation should be delayed until the maximum restoration of cardiac function has taken place. It is inadvisable to give quinidine sulphate preoperatively in an endeavor to abolish auricular fibrillation. It is difficult to restore normal sinus rhythm in the presence of active hyperthyroidism. Moreover, even with this result achieved, recurrence of auricular fibrillation during or after operation is the rule. It is wiser to try to control the heart rate with digitalis. In patients with auricular fibrillation, no cardiac enlargement and no heart failure it is unnecessary to give digitalis, because the auricular fibrillation causes them little circulatory embarrassment. In the majority of patients with auricular fibrillation complicating hyperthyroidism, there is a spontaneous restoration of normal sinus rhythm after subtotal thyroidectomy. If auricular fibrillation persists for two or three weeks following the operation, quinidine therapy should be instituted unless there is marked cardiac enlargement.

At times a damaged heart is further weakened by the presence of a severe secondary anemia occasioned by bleeding fibroids or hemorrhoids or some analogous condition. In these cases the anemia, as such, contributes to the heart failure, so that there is definite indication for operation to arrest bleeding. Preoperative treatment with bed rest, digitalis

and diuretics, and, particularly, transfusion to restore the normal oxygen-carrying capacity of the blood will bring about sufficient improvement to make operation possible. Such transfusions of citrated blood may be given very slowly by the drip method, even in the presence of heart failure. It is wiser to give small quantities, 250 c. c. daily, rather than to attempt to transfuse 500 c. c. at a time.

In all operations on patients with heart disease preoperative and post-operative care must be meticulous, and particular attention must be given to the prevention of preoperative anxiety and to cardiac strain incident to the excitement stage of anesthesia. A skilled anesthetist is the chief requirement. In selected cases local anesthesia may be best; in many avertin (tribromethanol) is most satisfactory. Chloroform, which is little used in this country, is best avoided because of its known tendency to induce ventricular fibrillation. Spinal anesthesia, as a rule, is not adapted to cardiac patients because of the drop in blood pressure that so often ensues. This is particularly marked in individuals with arterial hyper-tension, and in them spinal anesthesia is best avoided. Most cardiac patients tolerate ether well, and in most instances it is the best anesthetic.

Very commonly the nervous tension incident to the anticipation of the operation quickens the heart rate to a level higher than that provoked by the operation itself. This occurs particularly when the patient is brought into the operating room fully conscious and the anesthesia is started with the patient on the operating table. Again, the excitement stage of the anesthesia, whether it be nitrous oxide, ether or ethylene is always accom-panied by a great rise in heart rate which usually exceeds the maximum rate during operation, as well as that induced by preoperative excitement. Fluctuations in rate are closely linked to the depth of anesthesia; when the anesthesia becomes light, the heart rate quickens. In a placid individual, local anesthesia is often associated with a remarkable stability of heart rate. In tribromethanol anesthesia the excitement stage with rapid pulse is usually avoided. During the operation itself the heart rate is usually remarkably constant, and is little influenced by manipulations of tissues or viscera unless greater hemorrhage or shock set in (3). Anesthesia may cause abnormalities of cardiac mechanism such as extrasystoles or paroxys-mal auricular tachycardia (4). These are of little clinical significance for they almost invariably subside spontaneously.

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CHRONIC INTRAHEPATIC OBLITERATING CHOLANGITIS

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Clinicians are still confronted by difficulties in the diagnosis of cases of chronic icterus. Nevertheless, clinical experiences of many years, supported by the methods of X-ray diagnosis and the newer laboratory tests of liver function, have made it possible to reach a correct diagnosis in a considerable percentage of such cases. Moreover, where clinical observation at the bedside and laboratory methods both fail, surgical exploration will frequently clarify the situation. But there are cases which resist the combined efforts at diagnosis of internist and surgeon and find their final elucidation only after necropsy.

A detailed description of such observations may help the clinician in future diagnostic considerations and might also indicate certain problems in the pathogenesis of chronic icterus requiring more investigation. It is for these reasons that the following observation is reported.

CASE REPORT

History (L. M., Adm. 389131). The patient, a 37 year old butcher, was first admitted on February 14, 1934. Until eight months before he had been perfectly well. At that time he suffered from recurrent headaches over the left frontal region and nasal obstruction and went to the Post Graduate Hospital where he was given local treatment. Two months later he developed an upper respiratory infection characterized by slight non-productive cough, chilly sensations and fever. After three days in bed these symptoms disappeared completely and nasal obstruction cleared, but from then on he noted gradually progressive loss of weight.

Shortly afterwards he developed diarrhea one to two days each week, five to six times daily, with watery, brown, bloodless stools containing a small amount of glairy mucoid material. Gradually the diarrheal attacks became more frequent until two months before admission when the diarrhea became constant. There were neither bloody nor acholic stools. At this time his urine became dark in color and occasionally pruritus was present. His private doctor and friends noted that he was yellow and this jaundice had only slightly increased to the time of admission. His doctor gave him some pills (nature unknown) which stopped the diarrhea and he had continued to take the pills.

For the previous month he had had persistent "chest cold" with hoarseness and frequent dry cough productive only of a small amount of yellow-

ish sputum daily; there had been no hemoptysis. There had been occasional burning substernal pain after coughing. Since the onset of the present illness he had experienced moderately severe night sweats so that he had had to change his clothes at 2 A.M. almost every night. He denied any abdominal or other pain at any time and did not know whether he had had fever.

Examination. There was generalized icterus. The liver was palpated two to three fingers' breadth below the costal margin. Under it there was felt a vague, irregular, globular mass which was slightly tender. There was shock tenderness present over the right lobe of the liver. Blood pressure was 110 systolic and 75 diastolic.

Laboratory Data. Blood: hemoglobin, 82 per cent; white blood cells, 10,400; polymorphonuclear neutrophiles, 72 per cent; lymphocytes, 24 per cent; monocytes, 3 per cent; eosinophiles, 1 per cent. Urine: bilirubin and urobilin, 2 plus; albumin, negative; sediment contained 2 to 3 white blood cells. Stools: guaiac, 4 plus; urobilin, 4 plus. Blood chemistry: urea nitrogen, 12 mgm. per cent; cholesterol, 270 mgm. per cent; cholesterol ester, 120 mgm. per cent; icteric index, 25; Van den Bergh: direct delayed positive reaction, indirect 1:70,000 (i.e., 1.5 mgm. per cent bilirubin). The blood Wassermann test was negative.

Course. A provisional diagnosis was made of either a chemical hepatitis secondary to the administration of medication or an obstructive lesion involving the common duct. The latter diagnosis was considered much more likely, but it was qualified in that the obstructive lesion might be localized within the liver and bile passages. For this reason blood culture, agglutination and a bacteriologic study of the bile drainage was done.

Blood culture was negative. Agglutinations were negative for B. paratyphoid A and B. Duodenal drainage revealed many epithelial cells, a few gram positive diplococci. There were no white blood cells. Culture of duodenal contents disclosed streptococcus hemolyticus, streptococcus viridans and B. friedlaender.

Three days after admission he had a rise in temperature to 103.8°F. with chilly sensations. The tenderness of the liver increased.

Because of the persistent diarrhea with occult blood the stools were examined for amebae, but with negative results. The temperature after three days of elevation returned to normal. Sigmoidoscopy was performed and a rather deep ulcer was seen. Biopsy from the edge showed only mucosa without significant changes. He nevertheless was given emetine for eleven days.

Because of persistence of icterus, a suppurative lesion in the biliary radicles and probably in the liver was assumed to exist and exploratory laparotomy was recommended.

Operative Findings (by Dr. Colp). On opening the peritoneal cavity the liver was not found to be particularly enlarged. It was absolutely free

from the overlying diaphragm and no abnormal masses nor softened areas could be felt either in the right or left lobes. The liver appeared to be slightly fibrotic. The spleen was enlarged to about three times its normal size with a few adhesions about it. The gall-bladder was markedly distended and contained about 100 c.c. of thin, light brown bile full of shreds.

The cystic duct opened into the common and, on exposing the edematous gastrohepatic omentum, the common duct was found to be only slightly dilated but with engorged and enlarged hepatopetal veins occurring on its surface. Above the common bile duct in the region of the duodenum and occupying the foramen of Winslow were some large succulent lymph nodes. There was definite lymphadenitis in the region of the cystic duct. The size of these nodes varied, the largest measuring about 3 by 2 cm., the smallest 1 by 1 cm. It was thought that these enlarged nodes were sufficient to account for the partial obstruction of the common bile duct. Aspiration of the common bile duct yielded but little bile. The pancreas felt normal. There was no tumor in the duodenum or stomach.

A cholecystostomy was performed. A lymph node in the region of the cystic duct was excised and two punch biopsies were made from the left lobe of the liver.

After the operation the temperature rose to 103.4°F., dropped after two days and then remained between 100° and 101°F. for a week. On the tenth day he had a sudden rise to 104°F. and a chill, after which the temperature dropped to normal and remained so until his discharge. In spite of the external biliary drainage there was no change in the intensity of the icterus.

The punch biopsies of the liver showed bile thrombi within the intra- and inter-cellular bile capillaries. The small ducts were infiltrated by polymorphonuclear leucocytes and there were foci of liver cell degeneration. He was discharged unimproved.

Second Admission. The patient was readmitted five weeks later because of recurrence of fever, icterus, clay colored stools and dark urine since discharge. The drainage had continued to discharge yellow bile and daily dressings were required.

Examination. The patient appeared chronically ill, deeply icteric. The upper right rectus scar was healed except at its lower angle where there was a small opening discharging bile. The liver edge was palpable two fingers' breadth below the costal margin; there was no direct or indirect tenderness over the liver. A few fine râles were heard low in the right axilla and over the right base anteriorly. The blood pressure was 88 systolic and 58 diastolic.

Laboratory Data. Hemoglobin, 72 per cent; white blood cells, 10,900 with 62 per cent polymorphonuclear leucocytes. Stools: light brown; guaiac negative. Duodenal drainage yielded bile colored fluid with occasional epithelial cells, isolated white cells and cholesterol crystals. Blood

urea nitrogen, 15 mgm. per cent; cholesterol, 220 mgm. per cent; cholesterol ester 67 mgm. per cent; Van den Bergh, direct prompt positive reaction, indirect 1:40,000, 2.5 mgm. per cent bilirubin; icteric index, 60. Urine persistently showed bile and a trace of urobilin. Duodenal bile was positive for diastase and trypsin. Stool culture showed B. coli and staphylococcus albus. The blood Wassermann test was negative.

It was felt that the syndrome more closely approximated intrahepatic than common duct disease. This was supported by the fact that the icterus did not subside after gall-bladder drainage, and by the fact that the fistula showed a tendency to spontaneous closure which it would not have done in the presence of stasis in the common duct. Persistence of the icterus, leucocytosis, chills and fever were all consistent with the diagnosis of intrahepatic suppuration. The surgical consultant felt that no further surgical indication existed. The patient was treated symptomatically until the fistula closed spontaneously about a month after admission. He remained icteric, the stools were brown, he gained fourteen pounds in weight and on discharge felt fairly well. Five months later he re-entered the hospital.

Third Admission. The patient's condition was essentially the same as on his previous admissions. Echinococcus complement fixation test was made and found negative. The fragility test of the red blood cells showed normal limits of hemolysis. Because the stools were persistently guaiac positive, sigmoidoscopy and biopsy of the rectum were repeated but revealed no disease. X-ray examination of the gastro-intestinal tract showed no evidence of any organic lesion which might account for the melena. Because of the obscure nature of this patient's disease the stools were examined by the parasitologist of the hospital. It was his opinion that there was no evidence of parasitic disease. Biliary drainage yielded grossly normal bile containing many white cells. Culture revealed only yeasts and diphtheroid bacilli. It was the opinion of some members of the staff that a hepatic abscess might be present. Aspiration of the liver was therefore performed but no pus was encountered. Icterus fluctuated in intensity but never disappeared. The patient was kept on a high carbohydrate, low fat diet. At the end of seven weeks, no further information having been gained from the observation in the hospital, he was allowed to go home. On discharge it was the opinion of the staff that he was suffering from an intrahepatic infection of the bile ducts of low grade virulence and possibly a superimposed early cholangitic cirrhosis. Adequate drainage having once been established without relief of icterus, no further surgical indication was evident. The original cause of the intrahepatic disease remained a complete mystery.

During the following months, the patient was observed in the Follow-Up Clinic. His condition did not change very much, except that he developed clubbing of the fingers. He was admitted again because of hoarseness and a hemangioma of the left vocal cord was removed.

He was admitted for the fourth time two months later because of the same symptoms as on his previous admission.   The physical examination revealed nothing new except that a firm spleen was palpable one finger's breadth below the costal edge.   The Takata-Ara reaction was negative. He was afebrile while in the hospital.   A repetition of tests previously performed served only to confirm the previous diagnosis.

A gastro-intestinal X-ray series failed to reveal any abnormality in the small bowel.   The question of surgical biliary drainage was thoroughly discussed and decided in the negative.   There were two major objections to this operation.   In the first place, surgical drainage had never been demonstrated to be of any use in cases of hypertrophic biliary cirrhosis and, secondly, the patient's general condition was too poor to allow operation, even if such procedure might conceivably have been of any advantage.

The patient was finally sent home to be followed up in the Out-Patient Department.

The fifth and last admission occurred four months later.   He had been treated in the clinic with bile salts, vitamin D and a full diet.   With this therapy he gained 18 pounds and felt well.   His jaundice, however, remained unchanged.   About two months before admission the bile salts were stopped.   Several weeks later he began to lose weight, developed bleeding from the gums and ascites.   Several weeks before admission he received two mercupurin injections intramuscularly, following which there was marked diuresis with some temporary decrease in the size of the abdomen.

Examination.   He was now a thin, chronically ill-looking, prematurely grey male with deeply brown yellow skin and hugely distended abdomen. The sclerae were deeply icteric.   The lungs were clear.   The heart was normal.   The abdomen was greatly distended with fluid.   There was flatness in both flanks.   Slight tenderness existed in the right upper quadrant in the region of the liver which percussed about one finger's breadth below the costal margin.   The spleen appeared enlarged on percussion. There was a single dilated vein running vertically in the subcostal angle. There was definite clubbing of the fingers.   Feet and legs to above the knees were greatly swollen by pitting edema.   Blood pressure was 100 systolic and 54 diastolic.   Temperature was 98°F.; pulse 104 per minute; respirations 24 per minute.

Laboratory Data.   Hemoglobin was 58 per cent; white blood count 13,700; polymorphonuclear leucocytes 90 per cent; lymphocytes 7 per cent; monocytes 3 per cent.   Urine contained 4 plus bile, 1–20 urobilin and an occasional red blood cell.   Stool was brown, guaiac negative.   Blood urea nitrogen was 10 mgm. per cent; sugar 100 mgm. per cent; cholesterol 110 mgm. per cent; cholesterol ester 30 mgm. per cent; total protein 6.1 mgm. per cent; albumin 3.4 mgm. per cent; globulin 2.7 mgm. per cent; calcium 8.5 mgm. per cent; phosphorus 2.5 mgm. per cent; chlorides 630 mgm. per cent.   Icteric index was 145; acetone 37; Van den Bergh direct, promptly

positive reaction, indirect, 1:20,000, i.e. 5 mgm. per cent of bilirubin. Takata-Ara reaction was positive. Minimal amounts of tyrosine were found in the urine. Culture of biliary drainage showed staphylococcus aureus and albus, B. coli and yeasts.

Course. Paracentesis abdominis was done and 1900 c.c. of straw colored fluid were removed. The patient went rapidly downhill. There was persistent oozing of blood from the paracentesis wound; bleeding from the gums and bloody bowel movements appeared. Hemoglobin dropped from 58 per cent to 43 per cent. On the third day after admission he lapsed into cholemic stupor and in spite of continuous intravenous injections of glucose, liver extract and vitamin D, the patient died three and one-half years after his jaundice had first appeared.

NECROPSY FINDINGS

The body was that of a well developed, poorly nourished man of 37 years. It was still warm. Necropsy was performed one-half hour after death. The skin was olive-green; the sclerae were similarly colored. The fingers were thick; the nails were incurved and the eponychial areas were spongy, giving the appearance of early clubbing. The feet and lower portions of the legs pitted on pressure.

The panniculus adiposus was 0.5 cm. in thickness. On opening the peritoneal cavity, bloody fluid flowed freely forth. The anatomical findings summarized were as follows: hypertrophic cholangiolitic cirrhosis with splenomegaly and ascites; icterus; hemorrhage into intestines; pulmonary hemorrhages; edema of colon; mesenteric and lesser omental lymphadenitis; chronic valvular disease (rheumatic), mitral, aortic and tricuspid valves; arteriosclerosis of aorta, pulmonary arteries and of coronary arteries, without narrowing; pleural adhesions, left upper lobe; tuberculous primary infect, right lower lobe.

The *liver* weighed 2500 grams. It was large, green, finely granular and firm. The inferior edge was rounded, especially that of the left lobe. The capsule was smooth except for some pinkish-grey, granular material on the anterior surface of the right lobe. From the region of the falciform ligament and the region of the gall-bladder bed, grey, translucent, membranous tissue extended over and into the capsule for a short distance. The falciform ligament was appreciably thickened. Through the capsule the green liver substance, mottled by fine and coarse grey lines and small (0.5–1 mm.) yellow areas, could be seen. On section, the parenchyma did not bulge beyond the cut edge of the capsule. The liver was difficult to cut, felt firm to the knife and made a grating sound as the knife passed through it. The cut surface was green with numerous coarse and fine grey, translucent interlacing lines and small (0.5–1 mm.) opaque, yellow areas in most places surrounded by deep green liver substance. Lobular markings could not be distinguished anywhere. The larger and medium

portal fields were surrounded by a larger amount of yellow connective tissue than is usually seen.   Grey, translucent strands ran out from the walls of the medium hepatic veins to join similar strands coming through the liver parenchyma.   The smaller radicles of the portal fields could not be distinguished.   The liver substance itself, was divided into small (0.5–1 mm.) and somewhat larger (1–2 mm.) areas, by fine strands (0.2 mm. wide) of grey translucent tissue which joined coarser strands (0.5–2 mm. wide). In places they were apparently confluent.   The coarser strands formed interlacing bands through the liver, often encompassing liver already divided into small areas by finer greyish strands.   Some of the small areas of liver substance were homogeneous, green and smooth; others had small (0.5 mm.) opaque, yellow areas in their central portions.   The liver substance was in places raised above the surrounding grey, translucent strands. In some places, the greyish, translucent tissue was so abundant (numerous interlacing strands) that these portions of the cut surface appeared grey with pin-point green dots.   This was especially found beneath the capsule. The larger bile ducts within the liver contained turbid, yellow-brown bile in which dark brown granules were present.   The right and left hepatic ducts, the common hepatic duct and the common duct contained similar bile and granular material.   The mucosa of these ducts was thickened, yellowish-pink and somewhat finely granular.   The entire wall of the common hepatic and common ducts was thickened.   The lesser omentum contained many large (1–4 cm. in diameter) dark green lymph nodes which were elastic.   The cut surfaces were dark green, mottled by numerous small (0.5–1 mm.) greyish-yellow and some grey areas.   There was a large (4 cm.) node on either side of the common duct in the right border of the lesser omentum.   Between these the common duct was somewhat narrowed.   Above this region the common duct, common hepatic duct and hepatic ducts were somewhat widened.

Moderate pressure on the gall-bladder produced a free flow of turbid, yellow-brown bile through the papilla of Vater.   The common duct joined the pancreatic duct near the papilla of Vater; each opened into the duodenum by its own orifice.

The normal lobular architecture was abolished.   Islands of liver tissue of various sizes and shapes were separated by connective tissue strands. Some of these represented the thickened periportal ramifications of Glisson's capsule; others did not show any topographic relation to the periportal fields, although some of them branched off the former.   The septa consisted of thick connective tissue fibers and fibroblasts and were infiltrated by polymorphonuclear leucocytes, lymphocytes and plasma-cells. From their periphery stout fibers branched off into the adjacent liver tissue and surrounded small groups or even individual cells.   The fibers were accompanied by infiltrating inflammatory cells.   The liver cells at the periphery, thus surrounded, were often compressed and atrophic.   Often

they contained granular and globular bile pigment. The cytoplasm was
frequently vacuolated due to fat infiltration; occasionally it contained
hyalin eosinophilic granules and droplets. Throughout the liver cell
islands the intercellular bile capillaries were often filled with biliary casts.
Small groups were often observed of vaculated and icteric cells with
pycnotic or broken-up nuclei. Within such foci of necrobiotic cells leuco-
cytes accumulated. The periportal fields were, as mentioned before,
very much enlarged, due to connective tissue proliferation and inflamma-
tory cell infiltration. They included a conspicuous number of vascular
cross and longitudinal sections. Bile ducts, however, were inconspicuous.
In fact, frequently no lumen of a bile duct could be found in fields where
arterial and portal branches were most distinct (Fig. 1). Instead one saw
a cross section of a fibrous cord. These cords evidently represented the
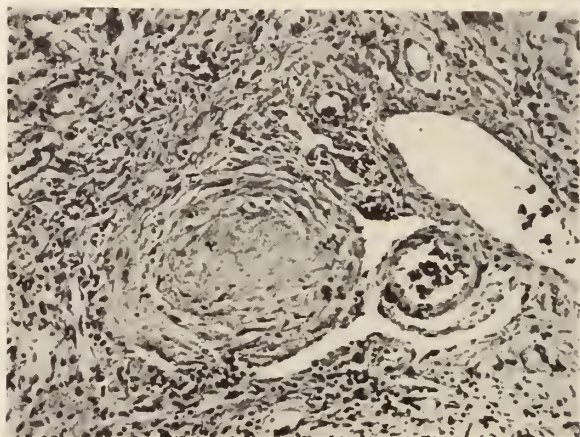
Fig. 1. Periportal field with branch of hepatic artery and portal vein, and com-
pletely occluded interlobular bile duct.

completely obliterated interlobular bile duct. The evolution of this
obliterating process was suggested by other fields (Figs. 2 and 3), which
showed bile ducts with tortuous or markedly narrowed lumina and flat-
tened epithelium surrounded by lamellated collagen fibers, infiltrated by
plasma-cells, lymphocytes and polymorphonuclear leucocytes.

The *gall-bladder* was markedly distended and contained turbid, yellow-
brown bile. The fundus projected 2 cm. beneath the inferior edge of the
liver where it was enveloped by membranous, fibrous adhesions binding it
to the anterior abdominal wall and the hepatic flexure of the colon.

The surface epithelium was mostly missing, due to post mortem desqua-
mation. The stroma of the mucosa showed an intense and diffuse infiltra-
tion with polymorphonuclear leucocytes, plasma-cells and lymphocytes.
The latter occasionally formed follicles. The muscularis was hypertrophic
and showed likewise infiltration with inflammatory cells.

The wall of the cystic and common duct also showed infiltration with inflammatory cells.

The *hepatic artery* was smooth and clear.   The portal vein at its point of origin and for some distance beyond this showed no changes.   About
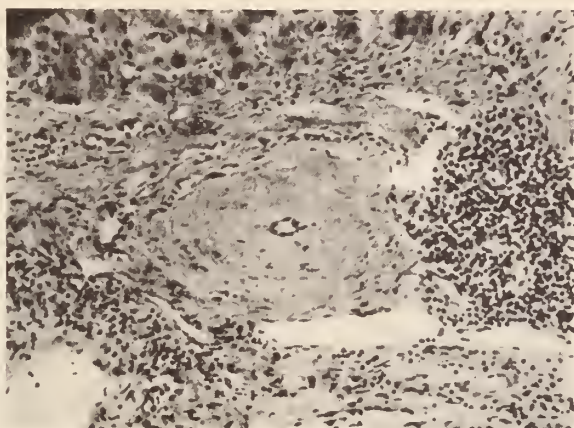
FIG. 2. Interlobular bile duct with excessively narrowed lumen
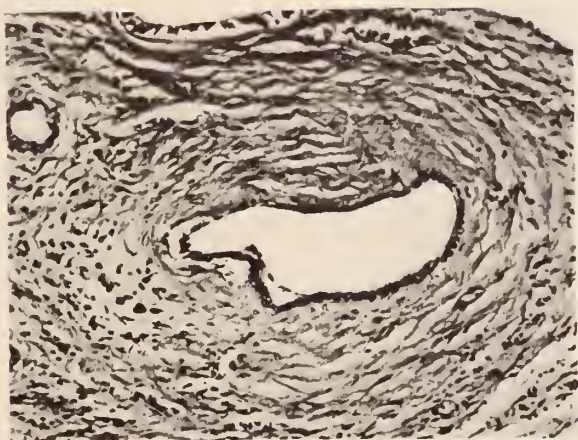
FIG. 3. Medium sized intrahepatic branch of hepatic duct with thickened wall infiltrated by inflammatory cells.   Epithelium flattened.

2 cm. from the porta hepatis the intima of the portal vein was yellowish-white (thickened).

The *spleen* weighed 400 grams.   Its capsule was smooth except for some scattered grey, stringy strands especially along the lower border.   Through it the red-brown substance of the spleen was visible.   The organ was firm. On section the cut surface was red-brown and homogeneous with numerous fine and medium trabeculae coursing through it.   The surface scraped

blood containing a small amount of pulp. The Malpighian follicles were easily seen as pin-point round and oval, greyish-white dots often surrounded by narrow (0.5 mm.) pink areas. The splenic vein and artery were smooth and clear.

Summary

Summarizing the clinical observations and necropsy findings, the case concerned a 37 year old white butcher who suffered for three and one-half years from a deep icterus with frequent febrile attacks. An obstruction of the extrahepatic bile ducts was ruled out by exploratory laparotomy. The severe icterus spoke against the diagnosis of hemolytic jaundice, which was further excluded by laboratory tests. A diffuse parenchymal disease was very unlikely because of the long duration of the disease. Moreover, the tests of liver function were consistently negative until the final stage of the sickness when they became positive, indicating a secondary involvement of the hepatic parenchyma. Clinical considerations suggested a diagnosis of an intrahepatic infection of the bile ducts of low grade virulence and possibly a superimposed biliary cirrhosis. No definite bacteriologic etiology was ascertained because only on one occasion were streptococcus viridans, streptococcus hemolyticus and B. friedlaender cultured from the duodenal bile.

Necropsy confirmed the absence of an evident obstruction of the large extrahepatic bile ducts.

Histologic examination of gall-bladder, common and hepatic ducts revealed chronic and acute inflammation. The intrahepatic medium-sized and small bile canaliculi were surrounded and markedly narrowed by dense connective tissue. The lumen was frequently completely occluded by fibrous tissue. The liver cells were deeply icteric and showed severe degeneration with occasional focal necrosis. The lobular structure was obliterated by connective tissue strands branching off the periportal fields, which showed chronic and acute inflammation. A diagnosis of biliary cirrhosis was justified.

The spleen was conspicuously large, presenting mainly the picture of chronic infectious splenic swelling on histologic examination.

Death was the result of severe anemia, caused by the hemorrhagic diathesis, and of liver insufficiency.

DISCUSSION

Inflammation of the intrahepatic bile ducts is either the result of an infection ascending through the large extrahepatic biliary channels or of a descending infection from the blood stream by bacteria excreted with the bile. Infection via the lymphatics has also to be considered.

It has furthermore been maintained (Rao (8), Hiyeda (3)) that organic and inorganic poisons (toluylenediamine and manganese salts) produce alterations of the epithelium of the intrahepatic bile ducts.

Investigators differ as to the significance of the hematogenous infection. Many French and German clinicians (Naunyn (7), Umber (11), Schottmueller (9)) have stressed the importance of this mode of infection. However, Aschoff (1) and recently La Manna (4, 5, and 6) have objected to the overestimation of the descending cholangitis. They have justly pointed out that some authors have wrongly diagnosed cholangitis because of the mere presence of periportal cell infiltration. Such lesions, however, may be entirely independent of a cholangitis. A diagnosis of cholangitis or cholangiolitis is justified only if inflammatory cells are found within the lumen and the wall of the bile canaliculi and if the inflammatory reaction is actually localized around the latter. A hematogenous origin of an intrahepatic cholangitis is acceptable only if the extrahepatic biliary system, including the gall-bladder, does not present any striking inflammation and if an extrahepatic mechanical obstruction does not exist. The pathologic-anatomic literature contains but few case records. E. Fraenkel (2) reports an observation of a 40 year old soldier who developed febrile icterus subsequent to a diarrhea of two weeks' duration. At necropsy the extrahepatic bile ducts and the gall-bladder were found without changes. Only the histologic examination revealed an extensive cholangitis and pericholangitis. A strain of B. paratyphoid A was cultured from the bile, which produced similar lesions when injected into guinea pigs. Siegmund (10) described eight cases of "independent intrahepatic cholangitis" which he regarded as the result of a hematogenous infection. In two of them, however, stones were found within the common duct and within the intrahepatic biliary channels. The bacteriologic examination of the bile in the other cases revealed staphylococcus aureus in one case, pneumococci and a green growing streptococcus in two other cases.

Cases of chronic icterus associated with intrahepatic cholangitis and cholangiolitis have been described as cholangitis lenta in the German literature. The term shall denote the existence of a chronic general bacterial infection with special localization within the biliary system analogous to the localization of the general bacterial infection on the heart valves in endocarditis lenta, (subacute bacterial endocarditis). Schottmueller and his school stress the particular rôle of streptococcus viridans in the etiology, but in several cases even repeated blood cultures were negative, or other bacteria were cultured from blood or bile. Furthermore, cases have been reported as cholangitis lenta in which an obstruction of the extrahepatic bile ducts was evidently responsible for an ascending infection, although in other observations a hematogenous infection was probable. Cholangitis lenta is therefore not synonymous with hematogenous intra-

hepatic cholangitis. Moreover, as La Manna has pointed out recently, the diagnosis of cholangitis lenta is anatomically not well defined.

In the case here reported the predominating pathology of the intrahepatic bile ducts speaks in favor of a hematogenous infection. But it cannot be ruled out that bacteria might have reached the liver by way of the large ducts and that the infection localized itself within the system of the small bile ducts. This is suggested by the initial intestinal symptoms and by the presence of chronic and acute inflammation of the gall-bladder and common duct. However this may be, the unusual feature of this case is the obliteration of many bile ducts which reminds one of the picture of obliterating bronchiolitis. The diagnosis of obliterating intrahepatic cholangitis is therefore in order.

The clinical syndrome of chronic icterus and hepato-splenomegaly without demonstrable obstruction of the extrahepatic bile ducts and only terminal ascites might suggest a diagnosis of Hanot's cirrhosis.

The gross anatomic findings of a large, icteric, smooth liver with conspicuous fibrosis and the splenomegaly support such a clinical diagnosis. Even the microscopic examination reveals the intralobular connective tissue proliferation and the pericellular fibrosis as described by Hanot. In fact, it should be pointed out only briefly that Hanot expressed the opinion that the peculiar liver cirrhosis described by him originated in an inflammation of the finer bile radicles. It is, however, questionable whether all his observations belonged to the same pathogenetic group. Nevertheless, among the observations of liver cirrhosis with chronic icterus, which are still frequently classified as Hanot's cirrhosis, the cholangiolitic obstructive liver cirrhosis certainly deserves recognition.

CONCLUSIONS

1. A case is presented of chronic icterus of three and one-half years' duration with frequent febrile attacks. A clinical diagnosis was made of an intrahepatic infection of the bile ducts of low grade virulence.

2. Autopsy disclosed a chronic obliterating intrahepatic cholangitis and a biliary cirrhosis.

3. The significance of intrahepatic cholangitis in the diagnosis of cases of chronic icterus and its relation to Hanot's cirrhosis is discussed.

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PERFORATION OF INTESTINE DUE TO ENTEROSTOMY TUBE; A HITHERTO UNDESCRIBED COMPLICATION OF ENTEROSTOMY WITH A REPORT OF TWO CASES

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The following two cases represent, as far as I can determine, the first recorded instances in the medical literature of intestinal perforation caused by an enterostomy tube introduced into the intestine by the surgeon for the purpose of intestinal drainage.

CASE REPORTS

Case 1. History (Adm. 386437). A male, 18 years of age, when first admitted to The Mount Sinai Hospital in August 1935, complained of recurrent abdominal cramps, rise of temperature and profuse sweats over a period of six weeks. He had three to four loose brown stools during this period. There was a similar episode three months before admission. He had not noticed blood, mucus or pus in the evacuations. There was an appreciable loss in weight. The abdominal pain was, for the most part, confined to the right lower quadrant.

Examination. The patient was a thin, undernourished, chronically ill young man. There was moderate tenderness in the right lower quadrant and a thickened area of intestine could be palpated. The stools consistently showed a 4 plus guaiac. Sigmoidoscopy revealed no disease. Gastro-intestinal X-ray examination showed an irregular stenosis of the terminal ileum with dilatation proximally with the colon from the cecum to the region of the splenic flexure showing loss of haustrations and marked disturbance in the mucosal pattern, indicative of an ulcerating lesion of the colon. Barium enema revealed an irregular stenosing lesion of the entire proximal half of the large bowel.

First Operation. Under general anesthesia the patient was explored through a left, mid-rectus incision. The terminal ileum, cecum and ascending colon were found thickened and edematous. The sigmoid appeared normal. The terminal ileum was divided one foot proximal to the ileocecal angle and a side-to-side ileosigmoidostomy was done. The patient developed a wound infection but otherwise made an uneventful recovery from this procedure.

He was readmitted one and a half months later for a colectomy. He had gained some weight but his stools still contained blood and he still

continued to have abdominal cramps, although on the whole his condition had improved considerably.

Second Operation. Under general anesthesia the scar of the previous laparotomy was excised, adhesions divided and separated, and the previously made ileosigmoidostomy identified. The terminal ileum, ascending, transverse and splenic flexures were excised after separating the omentum. The resection extended into the uppermost portion of the descending colon where the bowel appeared healthy. Retroperitoneal spaces were peritonealized. The wound was closed in layers without drainage except for rubber tissue drains placed at either angle superficially.

The patient appeared to be doing very well following this procedure until four days after operation when he developed signs of an intestinal obstruction, confirmed by a flat X-ray plate of the abdomen which showed distended small bowel with fluid levels.

Third Operation. Five days after the colectomy a laparotomy was performed through a right, mid-rectus incision. Numerous distended coils of the small intestine were encountered, bound down by recent adhesions. There was a large quantity of free fluid in the abdomen. The intestines were traced down to the region of the ileosigmoidostomy and it seemed that some loops ran under the mesentery of the ileum used in making this anastomosis. It was deemed inadvisable to disturb this mesentery for fear of compromising the blood supply. An enterostomy was performed in the most distal distended loop, using a number 26 French catheter, according to the method of Witzel. The tube was brought out through the lower angle of the incision.

Following this procedure the patient did well, the enterostomy functioned excellently, and the patient appeared to be well on the road to recovery with normal temperature and pulse five days after this operation. On the sixth day there was a repetition of the entire clinical picture but this time with a rise in temperature, cramps and abdominal tenderness. The enterostomy stopped draining and was irrigated a number of times without success, fluid being readily introduced but with no efflux. The patient now appeared extremely ill. The X-ray studies again supported the diagnosis of an intestinal obstruction and one week after the previous laparotomy, operation was again decided upon.

Fourth Operation. Through a suprapubic incision placed between the two previous ones, abdominal exploration revealed a diffusing fibrino-purulent peritonitis with pus and fibrin binding down loops of gut everywhere, particularly in the upper quadrants. In separating loops of intestine in an attempt to ascertain the cause of this widespread infection, a large abscess cavity was encountered in which the proximal two inches of the enterostomy tube were seen emerging through a free perforation in the antimesenteric portion of the ileum (Fig. 1). The tube was with-

drawn by an assistant and the perforation sewn over with catgut. The abdomen was closed without drainage. Culture of the pus revealed a B. coli, an enterococcus and a staphylococcus aureus.

Following this operation the patient passed a stormy and long course. He required a number of transfusions. The wound became badly infected and had to be laid widely open. A large quantity of pus discharged through the upper angle of the incision. It seemed to come from an in-

Fig. 1. Condition found at operation for supposed recurrence of intestinal obstruction. Note perforation of intestine by enterostomy tube. The drawing does not show the exudate and fibrin among the loops of small intestine.

tra-abdominal collection and was traced to the subphrenic region, being visualized by an injection of lipiodol. A counter incision for more dependent drainage was deemed advisable and this was done by excising the tenth rib in the post-axillary line and suturing the pleura to the diaphragm. A small rent in the pleura resulted in a pneumothorax. Subsequently, with a probe in the abdominal sinus, the subphrenic abscess was incised. Following this the patient made a gradual but prolonged recovery, being discharged well, approximately three months after the colectomy.

Case 2. History (Adm. 366245). A male, 57 years of age, was admitted to The Mount Sinai Hospital (Surgical Service of Dr. Edwin Beer, through whose courtesy this case is reported) with a history that, until a hemorrhoidectomy had been done a year previously, he had had bright red blood in his stools for a period of two years. Almost immediately following this operation he developed a bloody diarrhea. Two months before admission he noted blood and pus in the urine, and for two weeks just preceding entrance into the hospital there had been passage of sour material, fecal in nature, during micturition.

Examination. A sessile ulcerated mass on the posterior rectal wall about 8 cm. from the anus was seen by proctoscopic examination. The urine contained 3 plus albumin and was loaded with pus cells and red blood cells. The blood Wassermann test was negative. A small polyp was noted on sigmoidoscopy and was histologically shown to be acutely inflamed mucosa. A barium enema showed almost complete obstruction of the sigmoid a few inches proximal to its junction with the rectum. A cystogram showed an irregular indentation of the vertex of the bladder. Cystoscopy showed that in the left anterior wall of the bladder there was a fungating growth from which a biopsy revealed adenocarcinoma. A preoperative diagnosis of carcinoma of the sigmoid with involvement of the bladder was made.

Operation. After preparatory transfusion operation was performed and a large tumor was found in the sigmoid invading the left wall of the bladder. The involved bladder, as well as the sigmoid, were resected. An aseptic end-to-end anastomosis of the sigmoid was made and a transverse tube colostomy, according to the method of Witzel, was added to protect the newly formed anastomosis.

Postoperative Course. Following operation, despite fair drainage from the cystostomy tube, the patient had a marked febrile reaction and chills. The colostomy tube functioned on the second postoperative day. On the third postoperative day the patient became stuporous, exhibited twitchings about the mouth and extremities, and ceased.

Necropsy Findings. Only those facts pertinent to the discussion are reported. The upper tube (colostomy tube) ran through a serosal tunnel formed in the antimesenteric border of the transverse colon and was surrounded by the great omentum which was rolled together in the upper abdomen and was adherent to the anterior parietal peritoneum. Here, near the tube was a small collection of thick green pus. On further separating the great omentum, some fecal matter was found about the tube coming from a defect in the anterior wall and antimesenteric border of the transverse colon. This irregular defect was 1 cm. long by $1\frac{1}{2}$ cm. wide. The edges were thickened, soft, friable and edematous. The serosal tunnel was intact.

The necropsy revealed, in addition, an acute diffuse fibrinopurulent peri-

tonitis following perforation (decubitus ulcer of transverse colon at site of tube colostomy); acute hemorrhagic ulcerative cystitis, ascending pyelonephritis with multiple abscesses, pulmonary edema, atelectasis of both lower lobes, metastatic carcinoma of liver, and parenchymatous degeneration of the heart, liver and kidneys.

<div align="center">COMMENT</div>

Perforation of the intestinal wall by ingested foreign bodies is a well known clinical entity. Such perforations may be acute or chronic. Sharp objects, such as pins, needles, tacks, screws and the like, swallowed either accidentally or purposefully, are the most prone to cause this condition. Fishbone perforation of the intestinal tract with the formation either of a peri-intestinal abscess or a chronic granulomatous productive inflammatory tumor of the intestine or the surrounding mesentery has been described frequently. The production of a necrosis of the intestinal wall by pressure of rigid drainage material introduced from without into the abdominal cavity for purposes of drainage is one of the factors incident to postappendiceal and postoperative fecal fistulae. Perforation of the intestine by an indwelling catheter introduced by the surgeon for purposes of intestinal drainage has been hitherto undescribed and the cases herein reported are unique in this respect. The operation of enterostomy has become established as a well recognized surgical procedure for the relief of intestinal obstruction, particularly of the postoperative variety in which a plastic exudate or newly formed, filmy adhesions serve as the basis of the obstruction. It has proved a life-saving measure in this type of case. Enterostomy is also frequently employed proximal to an intestinal anastomosis to safeguard the suture line and to permit of the easy passage externally of fluid, feces and gas which might ordinarily be prevented from escaping by either edema or narrowing at the site of the anastomosis. Listed among the complications of enterostomy are peritonitis, due to the escape of infected intestinal contents at the time of operation; failure of the fistula to close spontaneously with a loss of intestinal juice and fluids of a highly irritating nature to the skin surrounding the fistula; and, finally, the necessity of occasionally being forced to perform a laparotomy to close the fistula, which may necessitate an intestinal resection. The two cases herein reported represent the rarest of enterostomy complications. In the first case the catheter perforated the intestinal wall, its proximal end lying free in the peritoneal cavity. This complication was entirely unsuspected, as evidenced by continued irrigating through the catheter, and was discovered accidentally at operation undertaken with the erroneous diagnosis of a recurrent intestinal obstruction. Fortunately, the condition was corrected in spite of a diffuse peritoneal infection and the patient recovered. In the second case, the enterostomy was performed in the transverse colon to protect an aseptic end-to-end anastomosis of the

sigmoid. In this case autopsy revealed a decubitus ulcer and perforation, probably due to a kinking of the tube with pressure necrosis of the gut wall. There was a well defined, punched out ulceration which was interpreted at post mortem as being caused by the enterostomy tube. While the two complications of enterostomy herein reported are extremely rare, the employment of enterostomy is sufficiently common to warrant taking such precautions as are feasible to safeguard against such accidents. For this purpose the catheter or tube employed should be of soft material, should lie as freely in the lumen of the gut as circumstances permit; the loop of intestine employed should be mobile, and for this reason it is deemed inadvisable to anchor the loop to the parietal peritoneum as is commonly done. The condition should be considered as a possible postoperative accident when an enterostomy has been done.

HODGKIN'S DISEASE OF THE GASTRO-INTESTINAL TRACT

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It is only within the past twenty-five years that Hodgkin's disease restricted to the gastro-intestinal tract has been recognized. In 1913 Schlagenhaufer (1) described cases of Hodgkin's disease in which the specific lesion was found only in the gastro-intestinal tract. Since that time a relatively small number of cases has been reported in the literature, not all of which will bear careful scrutiny. Thus, Hayden and Apfelbach (2) present data on twenty-six cases which, on closer analysis, are seen to present involvement of other organs, with a generalized lymphadenopathy in seven cases and involvement of the spleen and other viscera in ten. Mead (3) in an investigation of the subject in the post mortem material at the University of Minnesota Department of Pathology found three cases of isolated involvement of the gastro-intestinal tract in a series of 16,254 autopsies. Eighty cases of the generalized form of Hodgkin's disease were found in this series of autopsies, and in only one of these was there involvement of the gastro-intestinal tract. These facts indicate the background for the old time rule that the gastro-intestinal tract is immune to this disease and that this lack of involvement serves well in the differential diagnosis between lymphosarcoma and tuberculosis.

In recent years pathologists (4) in increasing numbers have leaned toward an inflammatory origin of Hodgkin's disease and have pointed out its many resemblances to tuberculosis. Moolten (5) has described a case of "primary lymphogranulomatosis of the lungs" with a lesion which may be considered as a primary complex not unlike that of tuberculosis. Similarly, the primary gastro-intestinal cases present what may be considered a primary gastro-intestinal complex.

However, these theoretical considerations, while of extreme interest, would not in themselves justify the publication of two cases of isolated Hodgkin's disease of the gastro-intestinal tract. The cases presented problems in clinical diagnosis and it is hoped that their presentation will draw attention to this rare condition and provide some diagnostic leads.

Case 1. History (Adm. 297520). A 46 year old white male was admitted with a one year history of epigastric pain which would occur three or four hours after meals and which was relieved by food. There had been several periods of remission in the interval between the time of onset of symptoms and the time of hospitalization. There had been no

vomiting nor evidence of gastric bleeding. There was a past history of diarrhea which had its onset about three years before hospitalization and which had persisted for a period of two years followed by a remission which ended with a recurrence of the diarrhea about one week before admission. At this time the patient was having about ten loose, non-bloody movements a day. There was an associated anorexia and the patient had lost about eighteen pounds in the past three years. There had been no appreciable loss in strength.

Examination. The patient was a well developed and well nourished white male who did not appear obviously ill. Systemic examination revealed no significant findings; abdominal and rectal examination were both negative. Examination of the stool showed no blood.

Course. Roentgen evidence of the gastro-intestinal tract two days after admission revealed a defect involving the antral portion of the stomach. Gastric tone was good, peristalsis increased with a slight delay in motility. The duodenum appeared normal. The roentgen diagnosis was carcinoma of the stomach (Fig. 1). Rehfuss test meal showed a free acid as high as 22 and a total acid of 44.

Five days later, on December 15, 1928, a partial gastrectomy was performed by Dr. A. A. Berg for "suspected carcinoma of the stomach." The surgeon described a diffuse, uniform induration of the lower two-thirds of the stomach with no area of sharp demarcation from the normal stomach. There was a marked enlargement of the periaortic glands as well as those of the lesser omentum and gastrocolic ligament.

The pathological report indicated the presence of a granulomatosis of the gastric mucosa and submucosa with ulceration. This was considered as possibly gastro-intestinal Hodgkin's disease. The lymph nodes were markedly hyperplastic.

This patient was observed carefully for a period of six years. In that time he continued to be in excellent health and showed no evidence of Hodgkin's disease in any other organ. He developed a postoperative anacidity.

Case 2. *History* (Adm. 375032). A 38 year old white woman had noted for the two years preceding her admission to the hospital increasing dyspnea and palpitation with exertion; this recently had appeared even at rest. There had been no edema. One year before admission she developed periumbilical pressure pain arising one-half to two hours after meals and especially after a heavy meal. This pain did not radiate and was not relieved by food or alkali. There was no night pain and she noted that the pain could definitely be brought on, or increased by, emotional distress. The pain was associated with nausea and both were relieved by induced vomiting. In addition, there had been vomiting on at least a half a dozen occasions in the first two months of her more recent illness. The vomitus contained no blood or food other than that of the most

recently eaten meal. She had been hospitalized in two other institutions where X-ray examination of the gastro-intestinal tract showed no abnormality. A progressive anemia led to repeated transfusions. With time the pain shifted to the left lower quadrant. There were no diarrhea, melena or fever. Amenorrhea developed six months before admission.

Fig. 1. Roentgenogram showing a constant filling defect in the prepyloric portion of the stomach.

There was a weight loss of twenty-three pounds in the year preceding admission, during which time she noted progressive weakness.

Examination. The patient appeared chronically ill, pallid and prostrated. The significant findings included a presystolic rumble with a loud snapping first sound in the mitral area. P2 was greater than A2. The abdomen was uniformly distended and was diffusely tender, especially so in the epigastrium and left lower quadrant. There was generalized re-

bound tenderness. There was no evidence of ascites and no organs were palpable. The fingers were clubbed. Blood pressure was 88 systolic and 58 diastolic. There was evidence of a secondary anemia with polynucleosis and slight shift to the left in the white blood count. The sedimentation time was 13 minutes. The stool showed a consistent presence of occult blood. Sigmoidoscopy showed no relevant findings. Fluoroscopy of the heart demonstrated a mitral configuration. The Mantoux test was positive with 1 mgm. of tuberculin. During her stay in the hospital she received many injections of a potent liver extract without apparent benefit. A Rehfuss test meal showed the highest free acid to be 30 with a total acid of 52. There was no blood in the gastric contents. A Janney test revealed the following:

TIME	BLOOD SUGAR	URINE SUGAR
	mgm. per 100 c. c.	
9:00 A.M.	65	0
9:30 A.M.	65	0
10:00 A.M.	80	0
11:00 A.M.	75	0
12:00 A.M.	75	0

The blood calcium was 7.8 mgm. per 100 c. c. Blood proteins were 4.8 mgm. per cent. The stool fat was 31 per cent dried matter. The clinical picture was strongly suggestive of the sprue syndrome.

X-ray examination of the chest showed no abnormalities. Roentgenologic examination of the gastro-intestinal tract revealed the following. The stomach and duodenum showed no abnormalities. Observations were made two, four, six, eight and ten hours after the ingestion of the opaque meal. On all the films the distal jejunum, and, perhaps, the proximal ileum, showed areas of constriction and dilatation. The margins of this portion of the small bowel were irregular and fuzzy in appearance. The findings were those seen in non-specific ulcerating enteritis. There was a delay in the small bowel and, ten hours after the ingestion of the barium meal, there was some still present in the jejunum and ileum (Fig. 2).

Despite all efforts to alleviate her condition the patient went rapidly downhill, lapsed into a coma fifty-four days after admission, and died.

Necropsy Findings. The heart revealed a chronic rheumatic pancarditis as well as involvement of the mitral and tricuspid valves with stenosis. There was massive embolization of the pulmonary arteries with early infarct formation and bilateral pleural effusions. In addition there was a granuloma of the jejunum due to Hodgkin's disease with caseating lymph nodes. About thirty centimeters below the ligament of Treitz there were found several granulomatous structures which had led to stricture forma-

tion and resulted in dilatation of the intervening intestinal wall. The lymph nodes of the corresponding segment of mesentery were greatly enlarged and showed areas of caseation. The omentum was adherent to these nodes. The mucosal surface was covered with numerous nodular

Fig. 2. Roentgenogram showing areas of constriction and dilatation of the distal jejunum and the proximal ileum. The margins of this portion of the small intestine are irregular and fuzzy in appearance.

excrescences and there were numerous subserous nodules. The histologic picture was that of Hodgkin's disease.

COMMENT

The two cases demonstrate the non-specific nature of the symptomatology, the clinical course and the roentgen appearances in Hodgkin's disease of the gastro-intestinal tract. The first case, with a typical his-

tory of peptic ulceration presented the very atypical feature of a painless diarrhea.   In addition, the stool showed the absence of occult blood.   One would not be justified at present in attempting any specific diagnosis in this case from the findings quoted above.   In the second case we have the clinical picture of malabsorption from the small intestine, associated with a roentgen picture which is in no way specific for the lesion found at necropsy.   We still await a more specific diagnostic procedure for the non-operative intra vitam diagnosis of this disease.

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SUBPHRENIC VAGOTOMY PLUS GASTRO-ENTEROSTOMY FOR DUODENAL ULCER

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The ultimate cause of peptic ulcer is, as yet, unknown. The most prominent theories are (1) the psychogenic, (2) the inflammatory (gastritis and duodenitis as fore-runners), (3) the functional or physiologic (hyperactive secretory and motor functions plus vascular spasm), (4) the ductless glandular (pituitary? adrenal?).

While the cause of ulcer is obscure, the mechanism by which ulcer is produced seems clearer. It is apparent that mechanical factors (various external irritants), the so-called "acid factor", and the tissue resistance or susceptibility are important. Of these three factors, the acid factor seems to be the crux of the problem since (1) ulcer occurs only in the acid areas, (2) it commences and continues only in the presence of free hydrochloric acid, (3) its occurrence in the esophagus and in a Meckel's diverticulum next to ectopic islets of gastric fundus glandular tissue is significant, (4) it is relieved by the medical therapies which continuously neutralize the acid (Sippy "milk drip"), (5) it is cured by a partial gastrectomy which is followed by achlorhydria and (6) there is an absence of recurrences after partial gastrectomy in the cases in which achlorhydria is present post-operatively.

The following studies on the acid factor have been carried on for several years. It was found early that patients with duodenal ulcer have a high preoperative acidity. This is particularly true of the amount and concentration of the acid during the longest interdigestive period, viz., the night. Interestingly enough, most gastric ulcer patients have a normal or low gastric secretion preoperatively. After partial gastrectomy, only one-half of the duodenal ulcer cases have achlorhydria (and this is a false or apparent one, due to neutralization) whereas practically all the gastric ulcer cases have a postoperative achlorhydria (a true one, as verified by the histamine and neutral red tests). Studies in the separate phases of gastric secretion, nervous and chemical, indicate that this acidity difference in duodenal and gastric ulcer is due to an inhibition of the acid-secreting cells in gastric ulcer, probably by a gastritis.

To date, none of the false or true achlorhydria cases (either in duodenal or gastric ulcer patients) have had a recurrence of ulcer. Approximately 3 per cent of the duodenal and recurrent gastro-jejunal ulcers which exhibited free hydrochloric acid after partial gastrectomy suffered from a

recurrent jejunal ulcer. This indicates the great value of the postoperative achlorhydria. Parenthetically, our studies, clinical, radiographic and hematologic, over a fifteen-year period, have demonstrated conclusively that this achlorhydria remains chronic and is in most instances harmless.

When my studies in gastric secretion demonstrated that the hypersecretion in duodenal ulcer was apparently due to hyperirritability of the vagus nerve (i.e. increase in the nervous and not in the chemical phase of gastric secretion) and also that this increased acidity could be completely abolished by atropine in the stomach after partial gastrectomy (and not in the intact stomach or in the stomach with a gastro-enterostomy), the idea occurred to the late Dr. Eugene Klein that it would be desirable and practical to add a high, subphrenic, anterior vagotomy to the operation of partial gastrectomy, particularly in those cases in which the preoperative acidity curve was high. Dr. A. A. Berg accordingly carried out Klein's excellent suggestion in 28 cases. The results have been most gratifying. The postoperative acidity in practically all of these cases fell shortly to an achlorhydria and the subsequent clinical course has been free from recurrences; (a complete report on this group is being prepared for publication). It should be noted that duodenal ulcer patients with a high preoperative acidity exhibit an achlorhydria after partial gastrectomy in only 25 per cent of the cases.

As a result of these considerations, the idea occurred to the author that it would perhaps be a valuable procedure in some cases of duodenal ulcer (particularly in the ulcers on the anterior, superior or inferior wall without deep penetration or marked pyloric obstruction) to perform a gastro-enterostomy, with or without local excision of the ulcer plus a high, subphrenic, anterior vagotomy.

Additional important data bearing on this proposition is being collected in this hospital by Drs. L. Ginzburg and S. Mage. They have found, in a study of the resected stomachs of patients who had a partial gastrectomy because of recurrent jejunal ulcer after gastro-enterostomy, that in practically all of these cases the original duodenal ulcer was healed. Unfortunately, while gastro-enterostomy seems to heal duodenal ulcer, it frequently causes a jejunal ulcer.

From the evidence already adduced here, it is obvious that, if the postoperative acidity after gastro-enterostomy were absent or even quite low, the occurrence of such postoperative jejunal ulcers would be greatly minimized. The usual gastro-enterostomy for duodenal ulcer fails to diminish the gastric acidity (Lewisohn and Ginzburg). This is probably responsible for the high incidence of gastro-jejunal ulcer after gastro-enterostomy. Following this line of reasoning, the author suggested the procedure of gastro-enterostomy plus vagotomy for duodenal ulcer in patients. This operation was then carried out on the service of Drs. Berg and Lewisohn

in two cases of rather severe duodenal ulcer with pyloric obstruction (one case operated on by Dr. S. Hirshfeld and the second by Dr. P. Klingenstein). It is one of the purposes of this communication to present the postoperative acidity curves and the subsequent course of the illness in these two cases.

Case 1. B. K., female, Adm. 304269, age 45. She complained of postprandial gnawing pains in the epigastrium with persistent vomiting for six weeks. Radiography revealed a duodenal ulcer with pyloric obstruction and an operation was advised. Dr. S. Hirshfeld found an indurated ulcer in the anterior wall of the duodenum immediately beyond the pylorus.
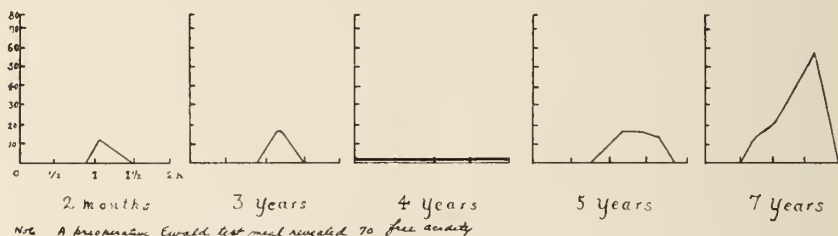
CHART 1

CHART 2

In accordance with the author's suggestion, he performed a suture, retrocolic, posterior gastro-enterostomy and divided the anterior vagus filaments at the cardia below the diaphragm. The test meal curves are given in the accompanying chart (Chart 1).

Her postoperative course has been observed for a period of eight years. With the exception of very slight postprandial pains on one occasion five months after the operation and again one year later, she has remained in excellent health.

Case 2. P. G., female, Adm. 3014415, age 24. Her illness commenced six years before her admission to the hospital. For a period of four months, she had rather severe epigastric pains one-half hour after meals. During the next six years she had, intermittently, short, mild, similar attacks. For one month before her admission, she had severe pain after meals,

heartburn, and frequent vomiting. Because of pyloric obstruction, as revealed by visible peristalsis and radiography, she was advised to undergo an operation. Dr. P. Klingenstein found an enormously dilated stomach and an indurated ulcer deep in the second portion of the duodenum, penetrating into the pancreas. He performed a typical suture posterior gastro-enterostomy and divided subphrenically the filaments of the anterior vagus nerve. The test meal curves are given in the accompanying chart (Chart 2).

Her subsequent course was observed from July, 1929 to March, 1937. She has gained forty pounds, has felt well, and has had no gastric symptoms during that period.

COMMENT

While no conclusions should be drawn from two cases, certain features are worthy of emphasis. The clinical course in both cases after the operation has been strikingly good through a fairly long period of observation. In the first case, the acid curve remained very low for five years and returned to normal only in the seventh year. The reduction in acidity in the second case was considerable in the third month and fourth year.

In dogs, bilateral thoracic vagotomy without gastro-enterostomy results in a marked decrease of the acidity, which, however, returns to normal in five months to two years (Van Zant). It would be of great interest to repeat these experiments using subphrenic vagotomy combined with gastro-enterostomy.

SUMMARY

1. The acid factor is of prime importance in the mechanism of peptic ulcer production.

2. Gastro-enterostomy usually cures duodenal ulcer but, unfortunately, causes jejunal ulcer in many instances.

3. Peptic ulcer patients with achlorhydria after partial gastrectomy do not have recurrent ulcers.

4. Since the hypersecretion in duodenal ulcer patients seems to depend on nervous influences, subphrenic anterior vagotomy has been suggested in addition to partial gastrectomy (E. Klein). The results of that operation are demonstrably good.

4. For a limited group of duodenal ulcers, gastro-enterostomy plus subphrenic anterior vagotomy is herein proposed. Two cases are described in which this procedure was performed. The results are encouraging and warrant giving this type of operation a fair trial in a larger number of cases.

MANAGEMENT OF ACUTE INTESTINAL OBSTRUCTION

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The high mortality in acute intestinal obstruction has long been a reproach to the surgeon. During the last decade, however, new developments in this field hold out a promise for the future reduction in the death rate. They are: (1) a clearer understanding of the chemical alterations in the body incident to intestinal obstruction; (2) improvement in the technique of continuous intravenous fluid administration which to a considerable degree permits the neutralization of such changes; (3) increased accuracy in diagnosis as a result of the better understanding of intra-intestinal gas distribution by means of X-ray studies; and, finally, (4) the continuous intraduodenal suction in accordance with the method developed by Wangensteen.

When confronted with a case suspected of mechanical ileus, it is important, first of all, to determine whether the site of occlusion is in the colon or the small intestine, for, as will be seen later, the mode of therapeutic approach differs materially in these two. While this differentiation can often be made by the history and physical findings, a study of the X-ray film will usually prove decisive. X-ray plates of the abdomen are, therefore, taken with the patient in the prone, supine, and, if possible, upright position, the latter to bring out the presence of fluid levels. If the patient is too sick to stand or sit up, a plate is taken in the lateral recumbent position with the same purpose in view. As has been pointed out in a previous article, the roentgenological criteria for establishing diagnosis of acute obstruction of the small bowel are: (1) the presence of gas in the small intestine sufficient in quantity to permit visualization; (2) the presence of fluid levels in the small intestine; (3) the absence or marked diminution of gas in the colon. In obstructions of the *colon* the distinguishing features are marked distension of the colon by the gas proximal to the site of obstruction, as well as the presence of fluid levels in the colon. If the simple plate of the abdomen shows changes leading to the suspicion of colonic obstruction, verification can be achieved by administration of a barium enema which is perfectly safe and will definitely establish the presence and position of the obstruction.

Caution should be exercised in diagnostic interpretation of the fluid obtained by gastric aspiration and the returns from enemata. In ob-

struction of the small intestine, small lumps of stool, fecal-colored fluid and fluid with a fecal odor may continue to be obtained for a number of days following the onset of obstruction. Furthermore, the passage of small quantities of gas after an enema does not rule out the presence of obstruction, especially in the small intestine. There is frequently a tendency to attach too much weight to this latter feature and to hesitate over the introduction of active measures.

Interpretation of the significance of gastric contents also has pitfalls. When the latter are definitely intestinal in character, they are indicative of the presence of either a mechanical or paralytic ileus. On the other hand, the author has on a number of occasions operated on patients whose bowel had rapidly become gangrenous, but whose gastric contents showed only a slight greenish tinge and were still acid. In colonic obstruction there may be only slight or no vomiting even in advanced cases. The author's experience has led him to view the presence of so-called fecal vomiting in large bowel obstruction as an evidence of some form of peritonitic complication.

Mechanical occlusion of the small intestine offers many more difficulties in diagnosis and operative indications than does acute colonic obstruction, and will be considered first. Incidently, in our experience, the overwhelming number of obstructions in the small intestine, exclusive of those caused by herniae, are due to bands or adhesions resulting from previous laparotomies. At Harlem Hospital, where such cases are numerous, it has become the rule to regard a patient with the scar of a previous laparotomy who is suffering from recurrent abdominal colic as suffering from intestinal obstruction until proved otherwise.

Until comparatively recently, the diagnosis of acute occlusion of the ileum or jejunum was synonymous with immediate operative intervention. In the last few years, Wangensteen has popularized his method of continuous duodenal syphonage with simultaneous and continuous intravenous administration of saline as a conservative form of therapy for this condition. This treatment is based upon the concept that the deleterious effects of intestinal obstruction are due to the continued loss of fluids and chlorides and to the effect of increasing intestinal distension upon the circulation of the mucosa of the bowel. The continuous administration of normal saline or Ringer's solution maintains the fluid-chloride balance and the continuous duodenal suction combats distension by preventing the gastric biliary pancreatic and intestinal secretions, as well as ingested gas, from being carried along the intestinal tract. It is felt that if such results are obtained and the patient carried along for a few days, certain angulating adhesive types of obstructions will right themselves. As would perhaps be anticipated, this type of treatment has proven most effective where the adhesions are of the fibrinous, incompletely organized type, which may go on to spontaneous resolution. Such favorable conditions are encoun-

tered most frequently in the immediate postoperative phase of a laparotomy. Its use in other types of small bowel obstruction (it is valueless in colonic occlusion) is limited by the fact that in a considerable number of these cases the obstruction is strangulatory in character. As the Wangensteen treatment cannot affect the relief of such obstructions, valuable time may be lost with progressive devitalization of the involved segment of bowel.

It is significant that at Harlem Hospital at least 20 per cent of ileal and jejunal obstructions are either actually or potentially strangulatory. Differentiation between a simple angulating or obturating and a strangulation ileus is exceedingly difficult, especially in the early stages. Signs suggestive of compromised bowel in intestinal obstruction are the presence of direct and rebound tenderness in the lower abdomen, a marked leukocytosis, and the presence of a vague, ill-defined mass or resistance beneath the scar. Incidentally, these signs appear only after considerable damage to the bowel has already occurred; on the other hand, these may all be absent, and it appears from observing patients on the wards who had at first refused operation, that an appearance of relative well-being may persist for a considerable length of time, even though strangulated bowel be present. This is especially the case when fluid is being continuously administered intravenously. Because of these difficulties, the Wangensteen type of therapy should be limited to (1) obstructions occurring in the *immediate* postoperative phase (q. v.); (2) instances where multiple laparotomies have already been performed for obstruction; for, in our experience, strangulation ileus and the secondary volvulus, which may complicate an originally simple obstruction, are much less common in patients with numerous broad fixing adhesions than in those with a few bands; (3) in obstruction within large multilocular hernial sacs where there is no sharp ring present, as in large postoperative eventrations; (4) obstructions secondary to or associated with acute intra-abdominal inflammatory conditions, especially in the pelvis; (5) early cases where the diagnosis is suspected, but cannot be definitely made; (6) as a valuable preoperative and postoperative adjuvant in cases of mechanical ileus subjected to laparotomy. During this course of treatment no attempt is made to increase intestinal peristalsis by either oral or parenteral medication. Such attempts are hazardous. The use of gentle colon irrigations is a better procedure; when effective, treatment is followed soon by the disappearance of abdominal cramps and by a clearing up of the intestinal contents which attain the character of clear duodenal contents. The effectiveness can also be checked by X-ray plates of the abdomen which in comparison with the original show a diminution of small bowel distention and the appearance of increase of gas in the colon.

In cases of small bowel obstruction where operation is necessary and feasible, the method of choice is to find and relieve the obstruction rather

than to perform an enterostomy. Enterostomy under local anesthesia will probably remain a method of last resort in those patients who arrive at such a late period in their illness that exploratory laparotomy is contra-indicated. The results in such cases, when strangulation is present, will, of course, always be bad but an occasional case of simple obstruction will be saved.

When exploration is to be performed, spinal anesthesia is the method of choice; it aids in the relaxation of the abdominal wall, the contraction of the bowel and the absence of straining, reduces the traumatization of distended bowel and thus facilitates the localization and relief of the ob-struction. Furthermore, under spinal anesthesia, relief of the obstruction is usually followed by a natural bowel evacuation while the patient is still on the table. Abdominal closure is also greatly facilitated. Moreover, pulmonary aspiration, always a potential danger with the use of inhalation anesthesia in such cases, is thus avoided. These advantages, however, are to a considerable extent counterbalanced by the depressant effect of spinal anesthesia, especially marked in such cases. Certain precautionary meas-ures should be observed. Intravenous infusion should be running before the anesthesia is administered. The dosage is to be kept down with 120 mgm. of novocaine at a maximum; 100 mgm. should suffice in most cases. As the site of obstruction is usually below the umbilicus, a high anesthesia is unnecessary and 2–3 c. c. of fluid are all that should be withdrawn and reinjected with only sufficient reaspiration to assure the presence of the needle in the subdural space. If signs of collapse and respiratory difficul-ties are encountered, it is a mistake to put the patient into a high Trendel-enburg position, as the weight of the distended intestine thrown against the diaphragm will further impede respiration. Furthermore, relaxation of the cardiac sphincter may occur and in the high Trendelenburg position may cause such rapid evacuation of the gastric contents by gravity, that fatal aspiration may occur. As a result of increased intestinal contraction following spinal anesthesia, considerable retrograde passage of fluid from the upper intestinal loops into the stomach may occur. It is for this reason that a nasal catheter should be left in the stomach and continuously aspirated by the anesthetist. This is especially important if general anes-thesia must be resorted to.

In the process of exploration for intestinal obstruction the localization of the site of occlusion and relief should be obtained with a minimum a-mount of manipulation. Attempts to define the site of obstruction by intra-abdominal palpation and evisceration of bowel are not only dangerous and provocative of shock, but also frequently fruitless. It is wisest to pick up a loop of collapsed bowel at the ileocecal junction and to follow it proxi-mally to the site of obstruction, to which it inevitably leads. Approach to the ileocecal angle is naturally simpler through a right-sided incision, and a right rectus incision is preferable. If the scar of a previous incision

is present on the right side, entrance is made mesial to it. Laparotomy through the site of an old scar is avoided for it may mean the necessity of dissecting away adherent bowel which is in no way involved in the obstruction, a procedure especially dangerous if the bowel is distended. Because of the tendency of the distended bowel proximal to the obstruction to crowd into the flanks and overlap the collapsed cecum and terminal ileum, it is frequently difficult to identify the latter by direct vision. The very best way to pick up the terminal ileum when it is not immediately detectable, is to pass the hand into the abdomen lateral to the ascending colon and then to sweep the fingers mesially and forward. The terminal ileum can usually be hooked up in this manner and followed proximally to the site of obstruction. Obturating obstructions, such as gallstones, intussusception or any intramural lesion, can easily be delivered into the wound and dealt with there. The greatest number of small bowel obstructions is, however, associated with bands and adhesions. Their general position having been defined, they are exposed and released in situ under direct vision. Attempts to deliver the bowel in such cases by blind manipulation may easily result in injury, especially at the site of constriction, with a resultant fecal spill. Constricting strangulating bands passing around loops of bowel should be divided between two ties. They will often retract themselves with a whip-like motion. In dividing angulating adhesions to the abdominal wall or pelvic viscera, it is wiser to proceed by sharp scalpel dissection well away from the bowel onto the site of adhesion. Dissection of adhesions should be limited to those whose division is absolutely necessary to relieve the obstruction and no further.

It should be remembered that a secondary volvulus of an obstructed segment is quite common and that after the release of the causative adhesions, it may still be necessary to deliver a mass of bowel out of the wound and untwist it. Under all circumstances the point of transition of dilated into collapsed bowel must be visualized as a complete mobilized zone and in strangulations both constriction grooves must be drawn up into the wound. It is our experience that most of the bands or adhesions causing obstruction are relatively easily released. Only rarely have we encountered such broad areas of adhesion that it was deemed wiser to desist from an attempt to relieve the obstruction in this way and to resort to entero-anastomosis or to ileostomy instead.

Ileostomy as a routine measure following the relief of an obstruction has not been our practice. Its use is limited to those cases where a small suspicious area of necrosis has been infolded, to protect suture lines, where peritonealization of a raw area has resulted in narrowing or kinking, and where it has not been deemed wise to deal directly with the causes of the obstruction. If ileostomy is performed, it is unwise to fix the bowel in the main operative wound. The infection and distension which are fre-

quent sequels may combine to cause some degree of dehiscence of the wound. Prolapse of the ileostomy may occur with angulation and knuckling and the possible development of a double-barrelled intestinal fistula which may require major procedures for its closure. Therefore, whenever possible, a small stab wound is made away from the main wound through which the ileostomy tube, which has been clamped close to the intestine, is drawn, after being passed through a piece of omentum, if this be feasible. Bowel and omentum are guided so that they come to lie against the parietal peritoneum at the site of exit of the tube. The preferred procedure is the Witzel operation, an 18 to 20 F. open end catheter being used. The selected loop of bowel is delivered through the wound which is then carefully padded off. In order to avoid spilling of intestinal contents, it is emptied by insertion of a large bore needle following which the delivered loop of bowel is clamped at either extremity with rubber covered clamps. The catheter is passed through an enlargement of the needle puncture hole. If the site of obstruction has been localized, the catheter should be passed orad. If a blind enterostomy is performed, too much attention should not be paid to this detail. In our opinion it is a matter of small moment which way the tube is passed, as it will drain only as long as there is stasis and pooling in the bowel. This is manifested by the fact that when the obstruction gradually relieves itself and normal intestinal peristalsis is reestablished, a tube which previously had been draining profusely will practically cease to discharge. It is at this time, incidentally, that we withdraw the tube. There is usually none or very slight drainage and closure occurs rapidly.

The determination of whether a badly compromised bowel is viable or not offers great difficulties. It seems illogical to keep the suspected bowel on the abdomen and to keep pouring warm saline over it. The ideal conditions for reestablishing circulation are with the bowel in the abdomen; and, when operating through a laparotomy wound, there is no objection to dropping the bowel back temporarily into the abdomen and covering the wound with a pad. After the desired length of time, the bowel can easily be withdrawn and reinspected.

When the bowel is found to be definitely non-viable, the choice lies between exteriorization and resection. Resection is preferable if the proximal area of the gangrenous bowel is more than five feet from the ileocecal angle, when the obstruction is of relatively short duration and if the patient's condition permits it. In many cases of strangulation by bands the progress is so rapid that the bowel becomes gangrenous before there is an opportunity for marked distension of the proximal loop to develop. On the proximal side it is important to carry the resection at least six inches to a foot from the site of gangrene. Distally, it will suffice to divide the bowel a few inches from the site of strangulation. A manoeuver which

considerably facilitates all suturing on the proximal distended side is to place two clamps at right angles to the bowel, one at the site of division, and the other four to six inches away. As the distal clamp is loosened, a suction tip is inserted, and the contents between it and the proximal clamp evacuated. In restoring continuity after resection, end-to-end anastomoses are avoided. Lateral suture anastomosis is preferred. However, lateral button anastomosis, performed by dropping one-half of the button through each open end of the bowel and cutting down upon them after closure of the cut ends, has proven quite successful. When the gangrenous segment involves the distal ileum and there is marked distension of the proximal bowel, with the patient's condition being poor, exteriorization of the gangrenous loop is, at times, the wisest procedure. Not infrequently, the gangrene will be found to extend to within an inch or two of the ileocecal angle so that exteriorization of the distal gangrenous portion is not possible without further mobilization. In such cases if the cecal and proximal ascending colon are easily mobilizable, a Mikulicz type of exteriorization may be performed. In other such cases where the retroperitoneal space has to be opened in order to mobilize the cecum and colon and an ileocolostomy is deemed inadvisable, it may be safer to invert the short distal end of the ileum into the cecum and to exteriorize the proximal loop as a single barrel. This has been done with excellent immediate results in a number of cases. In such a single-barrelled ileostomy, the discharge can be more easily controlled by tying a tube of the Paul variety into the lumen of the bowel. As soon as the patient's general condition permits, this can be short-circuited by an ileocolostomy with exclusion through a left-sided incision. All these exteriorization procedures mean a prolonged convalescence and morbidity and one or two secondary procedures. In gangrene of the distal ileum, however, they will often prove life-saving in otherwise apparently hopeless cases. Exteriorization of compromised segments high in the ileum or the jejunum will often give good immediate results but with a steady deterioration in the condition of the patient. In any instance of exteriorization, immediate steps to protect the skin should be taken. We have found that application of an aluminum paste around the skin margins is better than any other single method.

Obstruction in the Postoperative Phase. Intestinal obstruction in the immediate postoperative phase following laparotomy is practically always limited to the small bowel. It differs from the late types of postoperative obstruction in being the result of inflammatory agglutinative exudates which tend to undergo resolution and in being only very rarely strangulating in character. As has been already noted, these are the conditions which are ideal for the successful application of the Wangensteen method. In the last few years, the number of postoperative obstructions requiring

re-laparotomy has definitely fallen in most institutions, due to the more frequent application of this form of therapy. It should be instituted at once on the suspicion of the presence of an intestinal obstruction. If the symptoms of ileus are peritonitic or paralytic in origin, rather than mechanical, it is also the best available form of treatment. The urgent need of the often difficult differentiation between these varieties of ileus is, therefore, not as important now as it was previously.

In certain instances this type of treatment will not afford relief, especially in cases where the obstruction is around a drainage tract. In such events the best procedure is to perform an ileostomy low down in the ileum through a small incision placed low in the abdomen on the side opposite to the site of drainage. Exploration should never be undertaken for the localization and relief of the obstruction in such a case. Entrance into the drainage tract or separation of recent inflammatory adhesions either to relieve the obstruction, or through inadvertence, may easily lead to a fatal peritonitis. In postoperative obstruction following clean laparotomies which do not yield to the Wangensteen method of treatment, exploration and direct relief of the obstruction is permissible and may be simpler and followed by a lesser morbidity than performing enterostomy if the agglutinative or omental adhesions are limited. In the presence of broad adhesions it is wiser to do an ileostomy. It should be emphasised that symptoms of ileus postoperatively should always lead to a thorough inspection of the wound with the view of discovering possible subcutaneous evisceration.

Acute Obstructions of the Colon. In contrast to the diagnostic difficulties and surgical indications in obstruction of the small intestine, the management of acute colonic obstruction is relatively simple. This is due to the fact that obstruction of the large bowel, except in cases of sigmoidal volvulus, is practically always obturative in character. In the majority of cases a neoplasm of the bowel is the etiological factor. Diagnosis is relatively simple and can usually be made from the simple flat plate of the abdomen. Positive confirmation can be made by the use of a barium enema.

Excluding the rather rare cases of sigmoid volvulus, the operative treatment of acute colonic obstruction is *cecostomy*. There is little to be gained in attempting conservative therapy, as a cecostomy will be beneficial no matter what type of operative treatment may be undertaken subsequently. One of two types of cecostomy may be used; either a simple tube cecostomy or the exteriorization and fixation of a segment of the cecum and proximal ascending colon onto the abdominal wall. If the site of the obstruction or the predilection of the surgeon is such that a Mikulicz operation or one of its modifications is contemplated for the subsequent removal of the carcinomatous mass, a tube cecostomy will suffice. Sufficient decompression of the bowel can thus be obtained to permit such a procedure to be

safely executed at a later date. In such cases the tube cecostomy usually closes spontaneously and the patient will be spared another operation in addition to the two which the Mikulicz procedure entails. If, however, the situation of the tumor is such that immediate restoration of continuity should follow later resection, a large cecostomy should be performed in the upper part of the cecum and part of the ascending colon opposite the ileocecal opening, as emphasised by Dr. Berg. For the tube or small cecostomy a McBurney incision will suffice. Cecostomy in such instances can easily be performed under local anesthesia, if necessary. For the larger type of cecocolostomy an outer right rectus incision is preferable.

In some cases distension of the cecum is so great that its manipulation and delivery is fraught with danger of rupture and even the passage of the finest type of suture is followed by leakage through the puncture hole. In such cases it is wisest to pack the cecum off carefully on all sides and then to reduce intracecal tension by the insertion of a large bore needle. Before the needle is withdrawn, a purse-string suture is passed around it through the cecal wall and is tied as the needle is slowly withdrawn. In performing a tube cecostomy, a good-sized tube, about a 32–34 F., is used and should be directed up toward the ascending colon. When the exteriorization type of cecostomy is performed, the peritoneum should be sewn all around the delivered segment of bowel. The rest of the wound is closed very loosely and packed with gauze. Opening of the cecostomy should be delayed twenty-four hours, if possible. If distension of the exteriorized cecum again becomes marked, a needle may again be inserted to decompress it in the method described above.

Findings at secondary operations and at autopsies revealed the fact that a considerable number of sudden occlusions occurring in colon carcinoma is associated with actual or potential perforations in the region of the neoplasm, which have become sealed off. In addition, as has long been known, there are numerous tension ulcers in the bowel proximal to the obstruction. For fear of disturbing such limiting adhesions or causing perforation of a tension ulcer, it is rather dangerous to perform any type of exploration during the acute obstructive phase, especially to determine the site, fixation and operability of the tumor.

The only strangulatory type of obstruction encountered in the colon, as a rule, is *sigmoid volvulus*. This can usually be suspected clinically from the acuity and shortness of the onset and the rapid development of very marked distension. The flat plate will often clinch the diagnosis. If one is not sure, it is safe to make a right-sided incision which can be used for a cecostomy, if necessary. On opening the abdomen, the huge tremendously distended and discolored sigmoid is unmistakable. A generous abdominal incision should be made which allows the involved bowel to be delivered without undue traction, for the danger of rupture is very real. As has been stated above, the volvulus can be easily delivered through

either a left- or right-sided incision.   When the bowel has been delivered and untwisted, a tube should be passed up the rectum and guided into the sigmoid by the operator.   Evacuation and collapse of the enormously distended segment is thus achieved.   If the loop is gangrenous, exteriorization of the involved segment is indicated with the approximation of the afferent and efferent loops to make a spur.   Instead of fixing the bowel in the large main operative wound, it is wiser to deliver it through a lower left rectus incision, if operating from the right side, or through a left McBurney incision if operating through a left rectus incision.

THE INCIDENCE AND PROGNOSIS OF CARDIAC ARRHYTHMIAS IN CORONARY ARTERY THROMBOSIS

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In the course of an investigation of coronary artery thrombosis during the past few years we were impressed by the frequency of arrhythmias in this disease, and paid particular attention to their diagnostic and prognostic significance.

In a series of three hundred attacks of coronary artery thrombosis studied intensively, including frequent electrocardiograms, some type of arrhythmia other than premature beats occurred forty-six times in forty-two patients, an incidence of 14 per cent (Table 1). Premature beats were present in one quarter of all attacks. Although they were usually ventricular in origin, auricular beats were also observed, and frequently both types were associated (Fig. 1). Of the significant arrhythmias auricular fibrillation (Fig. 1) was the most common, being present twenty-two times. The others included paroxysmal tachycardia nine (Fig. 2), heart block, eight, of which five were complete and three incomplete (Figs. 3 and 4), auricular flutter three (Fig. 5), nodal rhythm one (Fig. 6), wandering pacemaker one. In addition simple prolongation of the A-V conduction time (P-R interval) occurred fifty times. In view of the emphasis usually placed on the occurrence of ventricular tachycardia in coronary thrombosis it is noteworthy that this arrhythmia was observed only once in our entire series, in spite of constant observation of the patients. Not uncommonly two or more types of arrhythmias occurred in the same patient at different periods or in close association (Fig. 1).

In half the cases the arrhythmias appeared within the first three days of the attack; in fact, an arrhythmia not infrequently ushered in an attack which was otherwise asymptomatic, and thus assumed diagnostic importance. Moreover, the arrhythmias were usually transitory, remitting spontaneously within one to three days. Often they were fleeting, lasting only minutes or a few hours; half the episodes of auricular fibrillation lasted less than twenty-four hours. The single instance of ventricular tachycardia observed disappeared after several hours. An exception to these statements was prolongation of the P-R interval which not infrequently occurred late and remained for a long period, or even permanently; simi-

TABLE I

TABLE I

Incidence and Mortality of Arrhythmias in Coronary Artery Thrombosis

	NUMBER		MORTALITY
Premature beats	77		22 (28.5 per cent)
Auricular		14	5
Ventricular		46	10
Auricular and ventricular		15	6
Nodal		2	1
Auricular fibrillation	22		10 (45.5 per cent)
Paroxysmal tachycardia	9		2 (22 per cent)
Auricular		3	0
Nodal		2	1
Ventricular		1	0
Undetermined		3	1
Heart block	8		4 (50 per cent)
Partial (dropped beats)		3	0
Complete		5	4
Auricular flutter	3		2 (66 5 per cent)
Nodal rhythm	3		0
Wandering pacemaker	1		0
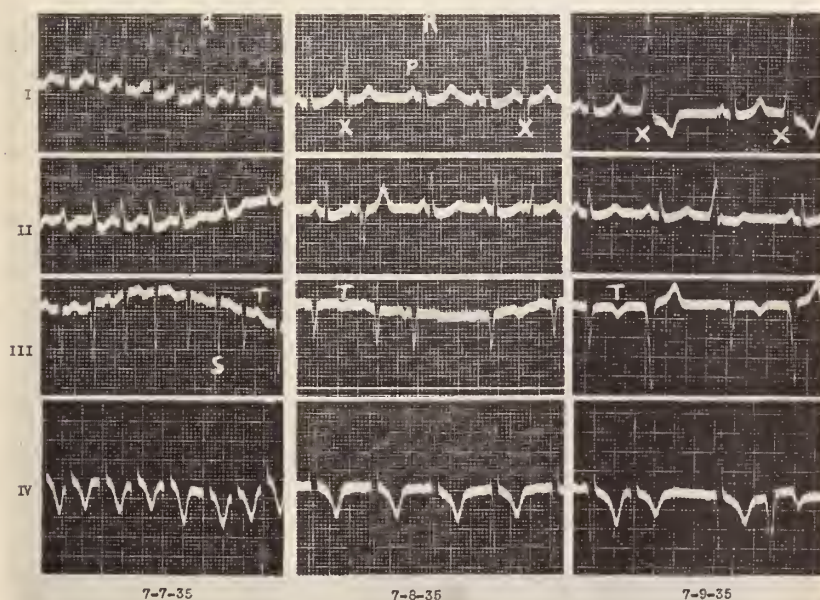
FIG. 1. J. G. Adm. 381891. Male, age 62. Coronary Thrombosis.

July 7, 1935. First day. Auricular fibrillation, as evidenced by rapid irregular ventricular complexes (RS) and absence of P-waves. Ventricular rate 150–200 per minute.

July 8, 1935. Second day. Resumption of sinus rhythm as indicated by return of P-waves, with numerous premature auricular contractions (x).

July 9, 1935. Third day. Sinus rhythm with numerous premature ventricular contractions (x) forming periods of bigeminal rhythm.

There has occurred a progressive inversion of the T-3 indicative of posterior wall infarction.
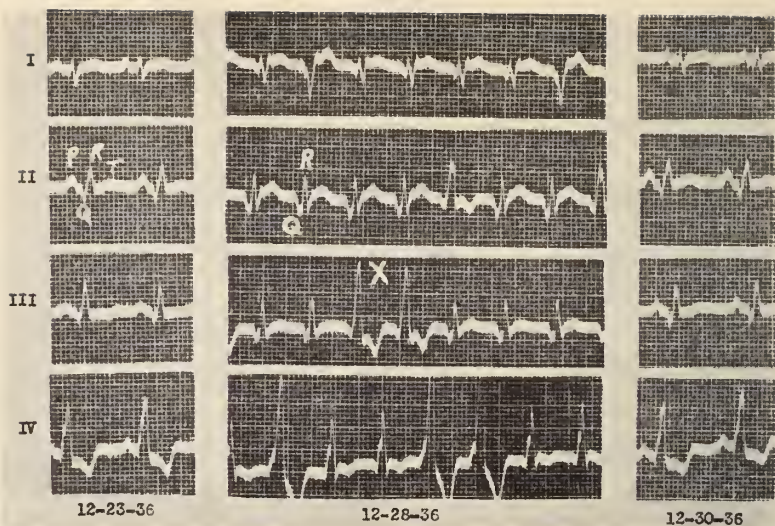
FIG. 2. L. D. Adm. 402671. Male, age 66. Coronary Thrombosis.

December 23, 1936. Second day. Regular sinus rhythm, rate 90–100 per minute.

December 28, 1936. Seventh day. Paroxysmal tachycardia, rate 140 per minute, nodal in origin because the ventricular complexes are similar in appearance to the record of the previous day and are not preceded by P-waves. Some of the complexes (x) are wider and taller than the others because of increase in degree of intraventricular conduction defect during the rapid rate.

The large Q-waves in Leads 2 and 3 and absent Q-wave in Lead 4 are seen in coronary thrombosis.
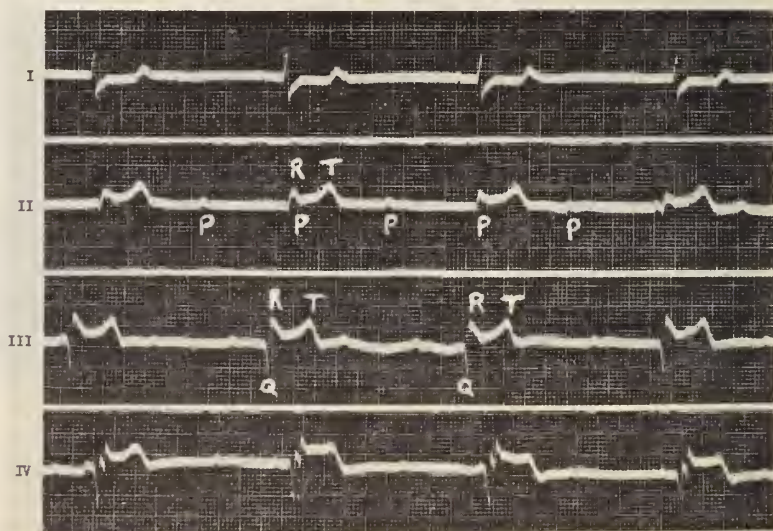
FIG. 3. I. L. Adm. 399108. Female, age 72. Coronary Thrombosis. Fourth day of attack. Complete A-V dissociation, auricular rate 65–75 per minute (P), ventricular rate 32 per minute and regular (QR). The large Q-3 and elevated R-T3 are characteristic of posterior wall infarction. Death on fifth day. Post mortem examination revealed right coronary thrombosis with massive infarction of posterior wall of both ventricles and septum.

larly complete heart block persisted, usually ending fatally. Sometimes an arrhythmia recurred, even after several weeks.

Since arrhythmias in coronary artery thrombosis are, as a rule, of short duration, it might be expected that they would not play an important rôle in the outcome of an attack.   Yet the mortality rate in patients with an arrhythmia was 40 per cent, as against 22 per cent in those with regular rhythm.   Furthermore the incidence of hypertension, cardiac enlargement and heart failure was over 80 per cent in cases with arrhythmias, which is
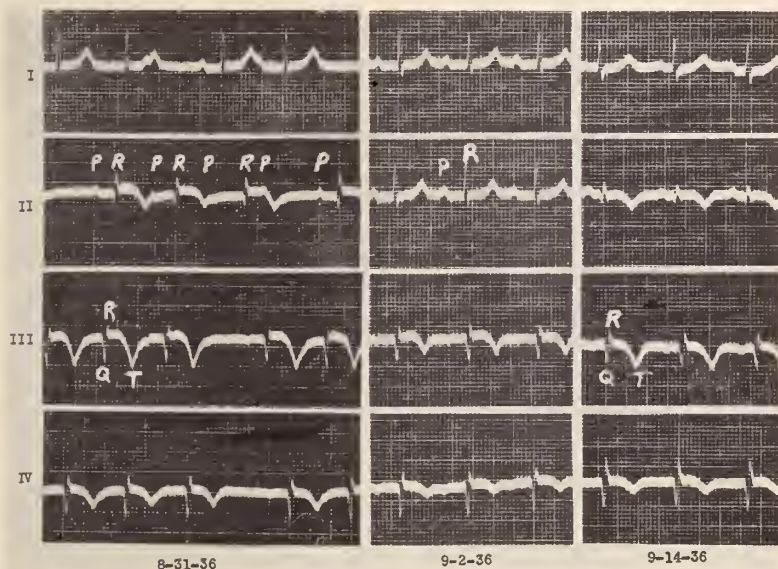
Fig. 4. D. R.   Adm. 397792.   Female, age 50.   Coronary Thrombosis.

August 31, 1936.   Third day.   Partial heart block, with frequent dropped beats (3:2 and 4:3).   Auricular rate 100 per minute.

September 2, 1936.   Fifth day.   Return to regular sinus rhythm, rate 85 per minute.   P-R interval still prolonged to 0.24 second.

September 14, 1936.   Seventeenth day.   P-R interval now normal, 0.16 second.

Large Q-3 and coveplane T-2 and T-3 indicative of infarction of posterior wall of left ventricle.

much higher than was obtained in the entire series.   It is thus apparent that arrhythmias occurred in the more severely ill patients; this fact, rather than the presence of the arrhythmia, probably explains the increased mortality.   For, in half the cases which ended fatally, death occurred some time after the cessation of the arrhythmia.   It is possible that the latter contributed to the severity of the heart failure in certain instances; however, heart failure usually was already present when the arrhythmia set in.

The increase in mortality rate in cases with arrhythmias was associated

with the presence of auricular fibrillation and complete block, with the deaths of almost half of the former and four out of five of the latter.   Furthermore, two of three cases of flutter ended fatally; in one of these fibrillation was also present.   The gravity of these arrhythmias resided in the fact that the cardiac rate was either very rapid, over 150, as in auricular fibrillation, or very slow, under 40, as in complete block.   It should be noted, however, that only two of the nine cases of paroxysmal tachycardia died, in spite of a rapid rate and the presence of cardiac enlargement and
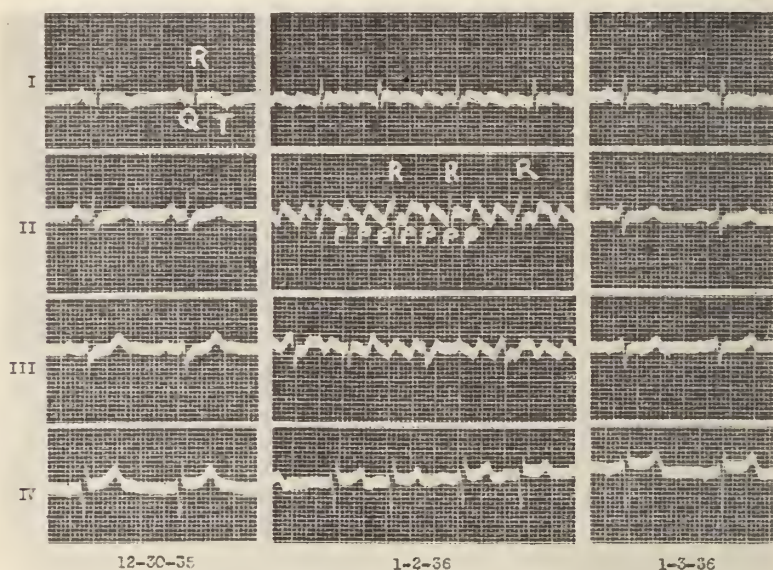
Fig. 5. S. L.   Adm. 328289.   Male, age 58.   Coronary Thrombosis.

December 30, 1935.   Twelfth day.   Regular sinus rhythm, rate 75 per minute.

January 2, 1936.   Fifteenth day.   Sudden appearance of auricular flutter, with irregular ventricular response.   Flutter rate (P) 330 per minute, ventricular rate (R) 85–135 per minute.

January 3, 1936.   Sixteenth day.   Resumption of regular sinus rhythm, rate 74 per minute.

The presence of a Q-1 and inverted T-1 is characteristic of infarction of the anterior wall of the left ventricle.

failure in all but one case.   This may be explained, however, by the very transient nature of these tachycardias, which lasted less than a day.

The cardiac rate, whether the rhythm was regular or not, proved a reliable prognostic factor.   Thus the mortality rate in patients whose heart rate did not go above 100 or below 40 was only 6 per cent.   When the rate was between 100 and 120, it was 29 per cent, and between 120 and 150, 54 per cent.   Correspondingly, there was an increase in cardiac enlargement and failure.   The reverse was true when the heart rate was

between 40 and 60.   In this group only two patients died, and heart failure was infrequent.

An attempt was made from the electrocardiogram and post mortem examination to correlate the type of arrhythmia with a specific lesion in the heart.   Only in heart block was there an association, for in such cases there was thrombosis of the right coronary artery with infarction of the posterior wall of the left ventricle, as previous investigators have noted. In other arrhythmias, as in the entire series, thrombosis was equally common in the right and left coronary arteries.   It is interesting to specu-
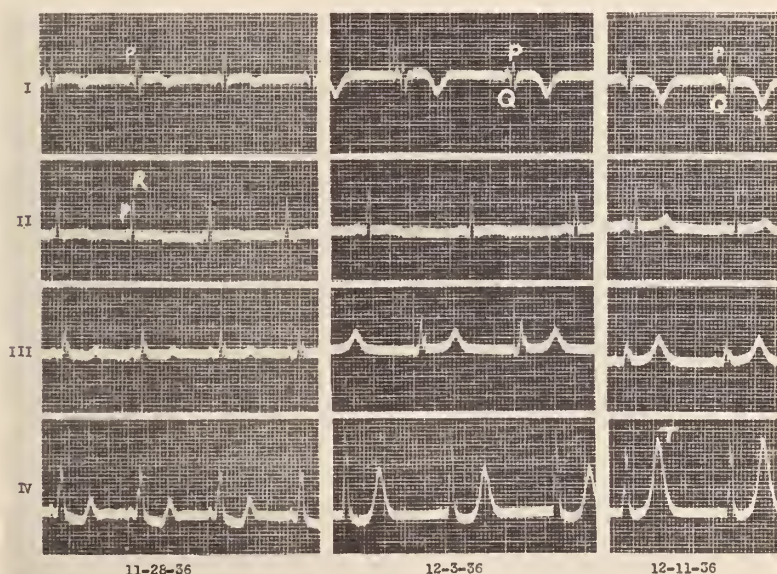
Fig. 6. A. Z.   Adm. 401640.   Male, age 47.   Coronary Thrombosis.

November 28, 1936.   Eighth day.   Nodal rhythm, rate 75 per minute.   The P-waves are diphasic in all leads and the P-R interval is very short, 0.08 second.

December 3, 1936.   Twenty-first day.   Sinus bradycardia rate 60 per minute. All the P-waves are upright and the P-R interval is 0.12 second.

The Q-1 and absent Q-4, the inverted T-1 and high upright T-4, are pathognomonic of infarction of the anterior wall of the left ventricle.

late on the pathogenesis of these arrhythmias.   A number of factors are probably at play.   When an area of heart muscle is infarcted it acts as an irritable focus from which impulses may arise, and, in addition, it disturbs conduction.   Furthermore, the nutrition and the metabolism of the heart as a whole suffer, with further impairment of conduction.   The cardiac output is diminished, and almost always the left heart fails, resulting in dilatation of the auricles, as evidenced by increase in size of the P-wave in the electrocardiogram following thrombosis.   The auricular dilatation is probably of great importance in initiating auricular fibrillation and

flutter. However, cardiac failure is not alone responsible, for the arrhythmia frequently disappeared in spite of the persistence of failure, or even when the latter had increased.

As we have seen, the outstanding feature of the arrhythmias is their short duration in most instances. It is therefore usually unnecessary to institute specific treatment. However, this rule cannot be adhered to under certain circumstances. For example, when complete heart block is associated with episodes of Adams-Stokes syndrome one is forced to use ephedrine or even adrenalin in spite of the danger of the use of these drugs in coronary thrombosis. Similarly when signs of heart failure appear and progress during auricular fibrillation with rapid ventricular rate which persists, it may be necessary to administer digitalis, although we believe that this drug is to be avoided as a rule in coronary thrombosis. This holds also for quinidine, which has been advocated often not only for the treatment, but also for the prevention of ventricular tachycardia. It will be remembered that this arrhythmia occurred only once in the entire series of three hundred cases, and then was very transient. It does not seem wise to use a drug, not without hazard, to attempt to prevent such a rare complication. Because of the lack of cases, we are unable to appraise its value when the arrhythmia persists.

HEMORRHAGIC INFARCTION OF FIBROMA OF PERITONEUM SIMULATING ACUTE APPENDICITIS

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Fibromata in general are common and more often not of great pathological interest, but a fibroma of the peritoneum or subperitoneal tissues appears to be rare and merits the following report.

History (Adm. 395117). A 32 year old Italian male was admitted to this hospital on July 27, 1936, with abdominal pain of three days' duration. The pain, acute in onset, was at first paraumbilical in location but had definitely localized in the right lower quadrant for the twenty-four hours preceding admission. The patient had been slightly nauseated but did not vomit. There was no constipation or diarrhea. His personal, family, and past history were irrelevant except for a gonorrheal infection six years previously which had responded to treatment. For the three to four weeks before admission he experienced some frequency but no other urinary symptoms.

Examination. The patient was a well developed and well nourished white male adult. His temperature was 100.0°F. and the pulse rate, 85 per minute. The abdomen was soft and not distended. There was direct tenderness in the right lower quadrant especially over McBurney's point. There was marked rebound tenderness but no rigidity. No herniae were present, and the genital organs appeared normal. On rectal examination, a firm exquisitely tender mass about 5 cm. by 3 cm. was palpated in the region of the right cul-de-sac. This was interpreted as being inflamed appendix with perhaps omentum wrapped about it. There were no other findings of significance. The urine analysis was negative. The preoperative diagnosis was acute appendicitis.

Operation. A five inch right lower mid-rectus muscle-splitting incision was made and the peritoneum opened. There was no free fluid in the peritoneal cavity. The cecum and appendix immediately came to view, presenting a completely normal appendix.

Upon exploring the pelvis a firm tumor about the size of an egg was felt in the lowermost portion of the cul-de-sac between the bladder and rectum. With the patient in Trendelenburg's position, the pelvis was exposed. In the region of the right pelvic brim, there was a split pea sized, pedunculated, pearly white, hard nodule which was removed for biopsy. On the

right side of the pelvis, just to one side of the midline, there was a firm, hemorrhagic, oval mass measuring about 4.5 cm. by 2.5 cm. by 2.5 cm. This mass was lying on the anterior wall of the rectum just as it dips down beneath the peritoneum, and it extended forward overlying the peritoneum on the inferior portion of the bladder (Fig. 1). It was covered with a moderate amount of fibrin and exudate of which a culture was taken. By gently insinuating the finger between the posterior peritoneum of the bladder and the mass itself, the latter was very easily mobilized and enucleated. No pedicle could be demonstrated. After enucleation, the bed
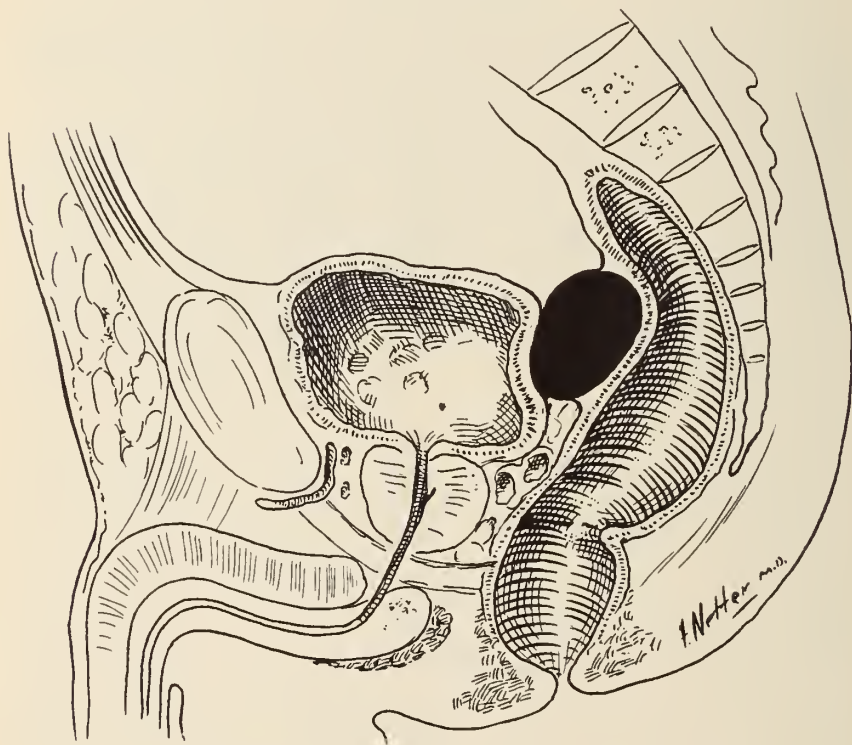
FIG. 1. Diagrammatic sketch to illustrate the location of the tumor.

in which it had lodged, namely, the anterior surface of the rectum and the posterior surface of the bladder, appeared intact but was inflamed, red, and granular. Whether this bed was lined with peritoneum could not be determined. A firm nodule which was located on the edge of the cavity from which the tumor had been removed was enucleated also for biopsy. The resultant cavity was then drained by means of a Penrose drain. Since the nature of the lesion was not accurately known, an appendectomy was not performed, in order to avoid the postoperative restrictions and possible complications incident to such a procedure.

Further careful search revealed no primary neoplasm of the viscera or other pathological changes. The operation was then terminated and the wound closed in layers.

Pathological Specimens. The tumor, examined immediately after the operation, had the gross appearance of a testicle. It was ellipsoidal in shape and measured 4.5 cm. by 2 cm. by 1.5 cm. (Fig. 2). The surface was smooth and shining and dark reddish purple in color. It felt quite firm but still elastic. On section, the appearance was that of an encapsulated tumor which was hemorrhagic. The cut surface was dark reddish purple mottled by grey areas in which were numerous punctate hemorrhages. It appeared to have a large component of fibrous tissue.

Microscopic examination revealed the characteristic structure of a fibroma with its relatively acellular connective tissue stroma. There was
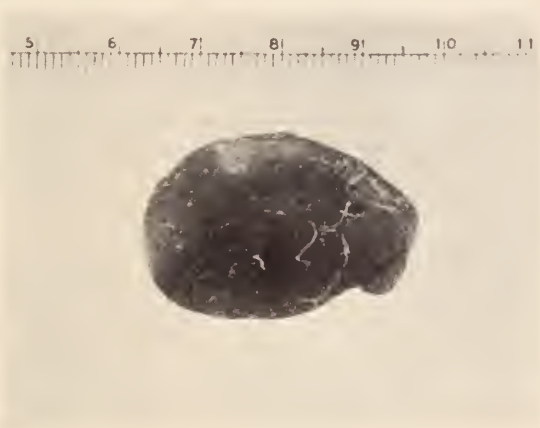
Fig. 2. Hemorrhagic fibroma of peritoneum. The projection from the right lower portion of the tumor is not a pedicle but is curled up peritoneum.

no distinct capsule, but its surface was lined by a layer of flattened meso-thelial cells. The veins throughout the whole tumor were dilated and full of blood. In some fields there was actual hemorrhage into the tissue. In many areas on the surface of the tumor, evidences of acute inflammation were present. Here the mesothelial covering was obscured by the super-ficial inflammation and exudation. The pathological report of Dr. P. Klemperer was, "Fibroma with excessive congestion of the veins as in early hemorrhagic infarction. Peritoneum with superficial inflammation." Special stains failed to reveal any nervous tissue elements or any muscle tissue other than in the blood vessel walls.

The small pedunculated nodule taken from the peritoneum in the region of the brim of the pelvis was of a comparable nature. It had a typical fibromatous structure and was covered with a layer of mesothelium. The

nodule from the wall of the cavity appeared to be a thickened area of peritoneum diffusely infiltrated with polymorphonuclear leucocytes.

Postoperative Course. Convalescence was entirely uneventful; the patient was discharged from the hospital on the thirteenth day and when last seen was well and asymptomatic.

<div align="center">DISCUSSION AND SUMMARY</div>

By the peritoneum (1) one means the serous membrane which lines the wall of the abdomen and is reflected over the contained viscera. It consists of two layers, the mesothelium and its connective tissue stroma. We believe that the hemorrhagic fibroma and the small pedunculated fibroma arose from the connective tissue component of the peritoneum, and hence have classified the lesions as fibromata of the peritoneum.

Whether the larger tumor was originally pedunculated and then dropped down into the pelvis after being twisted and infarcted, or whether it arose from the peritoneum over the rectum, where it was found, cannot be stated with any certainty. It was only evident that its blood supply had been interfered with, and that the infarction and secondary inflammation of the surrounding peritoneum had given the patient his symptoms. The increased frequency of urination for three to four weeks suggests the duration of the acute process.

Nothnagel (2) states that fibromata are rare and must be distinguished from so-called fibrous peritonitis, in which the peritoneum is uniformly covered with fibrous tissue overgrowths. A review of the available recent literature disclosed no record of a lesion which was classified as a fibroma of the peritoneum. Subserous fibromyomata of the uterus which have become pedunculated and then secondarily implanted on the peritoneum are well known (3, 4, 5). A variety of other types of tumors, including myxofibroma and xanthofibroma, have been described (6, 7). Primary sarcoma of the peritoneum has been reported, but this, too, is quite rare (8, 9). A report of a benign primary fibrous tissue tumor was found in the literature. It was a case of papillomatosis of the peritoneum, discovered as an incidental finding at autopsy (10). A number of tumors of the mesentery, including fibromata, were recently reviewed (11) but in no way resemble this case.

The case reported is one of hemorrhagic infarction of a fibroma of the peritoneum. Clinically, it simulated acute appendicitis.

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ABSCESS OF LUNG RECURRING IN DIFFERENT SITES

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The following case of abscess of the lung involving different sites on three separate occasions is reported because of its unusual clinical features.

CASE REPORT

History (Adm. 402427). The patient, a forty-eight year old woman, single, was first admitted to The Mount Sinai Hospital on November 27, 1932. She gave a history of pulmonary disease dating back twenty-five years prior to her first admission to the hospital. The pulmonary symptoms appeared following an adenoidectomy and a severe postoperative hemorrhage. She remained weak for several months, and then developed "pneumonia" which subsided in a short time. About a year later, she began to cough and expectorate rather large amounts of sputum which had a foul odor. This persisted for almost two years, during which time she developed pleurisy with effusion. She improved at first, but six months later began to have hemoptyses. The suspicion of tuberculosis was entertained, but repeated sputum examinations were negative for tubercle bacilli. For a long period of time she remained in good health. Three years before admission she began to cough with foul sputum.

On August 13, 1929, the patient was admitted to the Beekman Street Hospital. Just prior to that date, a roentgen examination of the chest was reported as showing "a clouding of the right base, the central portion of which was occupied by a small area having the appearance of a cavity, the lower half of which was filled with fluid. An interlobar pleural septal thickening was noted between the right middle and lower lobes." The roentgen examination in the Beekman Street Hospital confirmed these findings. A bronchoscopy revealed "a stenosis of the right lower lobe bronchus, the lumen of the bronchus being reduced to one-third of its normal size. Foul, thick pus was noted in small quantities from below." Postural drainage was instituted, and the patient was discharged on September 10, 1929. At this time the cough was less severe, and the abscess cavity was reduced in size, as shown by roentgen examination.

In October, 1932, six weeks before admission to The Mount Sinai Hospital, there was a recurrence of cough followed by a slight odor to the breath, and a mild, sticking pain behind the left shoulder. Three weeks later there developed high fever and profuse expectoration of foul sputum.

Examination. On examination on November 27, 1932, the patient appeared acutely ill. The temperature was 101°F. The breath was foul. Examination of the lungs showed dullness, slight suppression of breath sounds and, after coughing, numerous crackling râles in the left infraclavicular region. The fingers were clubbed. These findings suggested an abscess in the left upper lobe. The hemoglobin was 70 per cent, the white blood cell count 10,900 with 70 per cent polymorphonuclear neutrophiles. The blood pressure was 82 systolic and 56 diastolic. The blood Wassermann and Kahn tests and the urine were negative. The sputum exami-
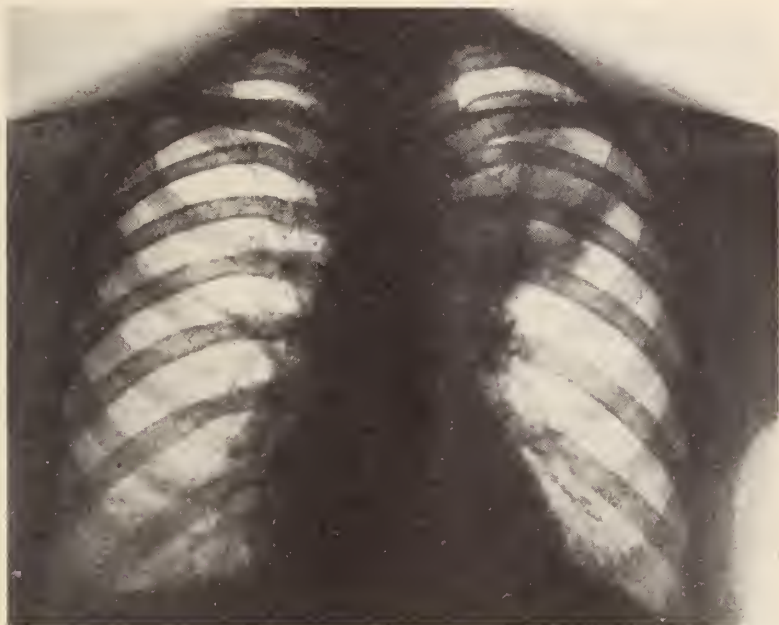
FIG. 1. Roentgenogram taken November 28, 1932 showing abscess cavity in the left upper lobe.

nation was negative for tubercle bacilli. The roentgen examination of the chest showed "an infiltration in the left lung which extended from the level of the first to the third ribs anteriorly. The infiltration extended laterally as far as the midclavicular line. Within the infiltrated area there was a circular cavity about three-fourths of an inch in diameter with probably a smaller one just above it." The roentgen appearance was that of a lung abscess (Fig. 1). In the right lower lobe there appeared to be a resolving pneumonia.

Course. After the first two days in the hospital, the patient was afebrile. Fluoroscopic examination of the chest at the end of the second

week of hospitalization, on December 9, 1932, showed relatively little infiltration about a small cavity in the left upper lobe, the site of a much larger lesion at the time of admission. The physical findings were essentially negative. A roentgen examination of the chest on December 21, 1932, showed "a marked decrease in the area of infiltration previously reported in the left upper lobe. The cavity had also decreased in size, so that it was faintly indicated and was about one-half inch in diameter. The infiltrations in the right lower lobe were also decreased."

The largest amount of sputum per day was three ounces. This was at first foul and blood streaked. The sputum gradually diminished in amount and lost its foul odor, and by the fourth week of hospitalization there was no sputum. Repeated sputum examinations were negative for tubercle bacilli. There was no record of a bronchoscopy. The patient was discharged on December 25, 1932.

When seen in the Follow-Up Clinic on February 2, 1933, physical examination was essentially negative and the patient was symptom free. Fluoroscopic examination of the chest showed fibrotic strands at the site of the recent abscess in the left upper lobe. On April 20, 1933, there was a small hemoptysis. On October 12, 1933, it was noted that the patient had an upper respiratory infection with some cough and expectoration. Physical and fluoroscopic examination of the lungs were negative. On April 12, 1934, the patient was again symptom free. Fluoroscopic examination of the chest showed persistence of some infiltration in the right lower lobe. The left lung was entirely negative.

Second Admission. The patient was readmitted to the hospital on December 17, 1936. She had no complaints except for frequent head colds, until about October 1936, at which time she developed an upper respiratory infection. In the early part of December 1936, she noticed slight pain in the right chest on breathing running from the region of the nipple around to the axilla and through to the back at about the level of the angle of the scapula. This was accompanied by malaise and a "grippy" feeling. About two days after the onset of the chest pain, she began to cough. Two days later she noted foul, blood streaked sputum which rapidly increased in amount filling two sputum cups daily. On one occasion she coughed up about two tablespoonsful of dark blood mixed with sputum. Her temperature ranged between 100° and 102°F., occasionally accompanied by chilly sensations.

Examination. The patient did not look very ill. The temperature was 101.6°F.; the pulse rate, 88 per minute. Examination of the chest showed dullness at the right base from the angle of the scapula down posteriorly and in the lower axilla, with diminished breath sounds and fremitus and many fine crackling râles in this region. There was moderate clubbing of the fingers. The hemoglobin was 83 per cent, and the white blood cell

count was 17,000 with 81 per cent polymorphonuclear neutrophiles.   The blood pressure was 85 systolic and 60 diastolic.   The sputum examination was negative for tubercle bacilli and the higher bacilli.   It was noted that the odor of the sputum was acrid and more suggestive of the odor in chronic bronchiectasis.   Culture of the sputum revealed a mixture of organisms—staphylococcus albus and aureus, enterococcus, streptococcus hemolyticus, diphtheroids, bacillus alkaligenes, and bacillus friedlaender. The blood urea was 10 mgm. per cent, and the blood sugar 105 mgm. per cent.   The blood Wassermann and Kahn tests were negative.   The sedi-
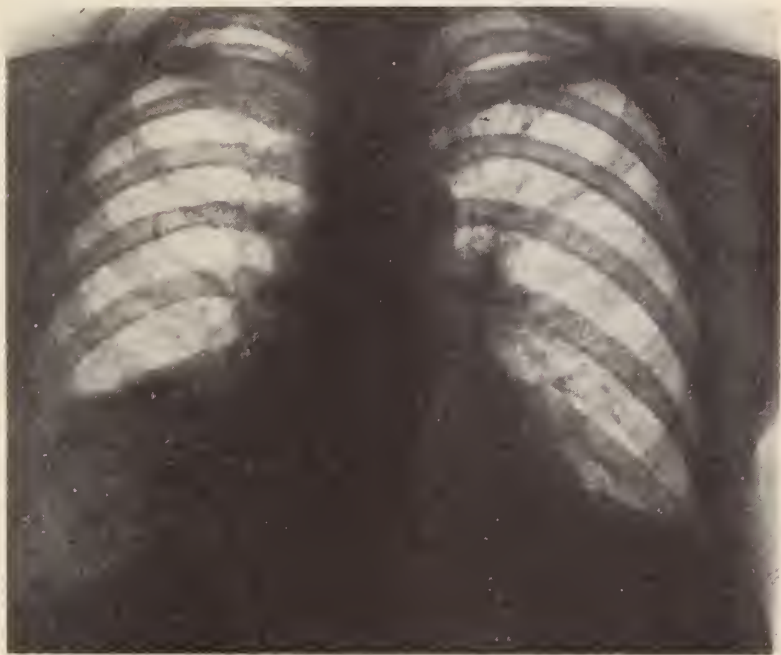
Fig. 2. Roentgenogram taken December 17, 1936 showing consolidation of the right middle lobe.   There is no evidence of abscess of the left upper lobe.

mentation time was 45 minutes.   Roengten examination of the chest showed "a complete consolidation of the right middle lobe.   There still remained some contraction of the right lower lobe over which there was a thickening of the pleura, in the anterolateral portion of which there was evidence of fibrosis.   There was no residual infiltration in the left upper lobe" (Figs. 2 and 3).

Course.   Roengten examination of the chest on December 23, 1936 showed no change, and Dr. Rabin reported that the main pathological process was in the middle lobe which was densely consolidated.   A bron-

choscopy on December 21, 1936 by Dr. Irving Goldman disclosed foul fecal smelling pus appearing from the right middle lobe orifice which was markedly red and edematous. On December 24, 1936, after a week of hospitalization, the patient was afebrile. At this time she was expectorating about ten ounces of purulent sputum daily, and on several occasions the sputum was noted to be very foul. Postural drainage was instituted. The cough diminished, but the amount of sputum continued at about ten ounces
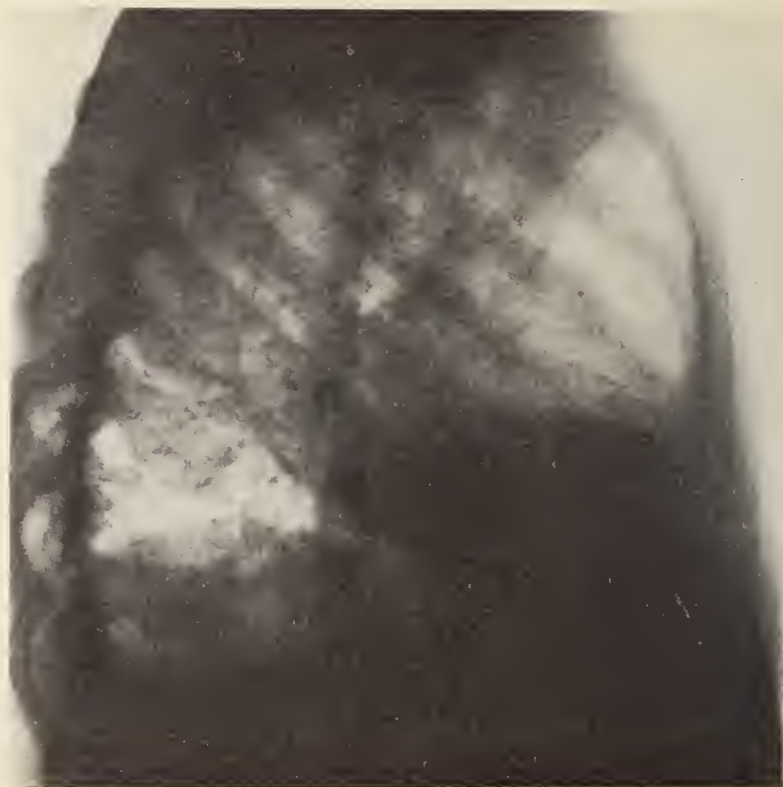
Fig. 3. Lateral view of roentgenogram taken December 17, 1936 showing consolidation to be in the right middle lobe.

a day and became less frequently foul. Examination of the nasal accessory sinuses by Dr. Irving Goldman showed a chronic, low grade sinusitis. Roengten examination of the sinuses showed a slight clouding of the antra on both sides with evidence of thickening of the lining membrane. The remaining sinuses were negative. Examination of the teeth showed no active focus of infection. Roengten examination of the lungs on December 31, 1936 showed "a small fluid level in the upper portion of the consolidated middle lobe. In the axillary portion of the lobe there were also

a few small areas of increased aeration which had the appearance of small cavities within the lobe."

On January 4, 1937, bronchoscopy was repeated.   At this time much less edema was noted about the middle lobe orifice.   There was no odor of the pus which came from the axillary division of the middle lobe bronchus.   There was some narrowing of the right lower lobe bronchus but within normal variations.   A culture of the pus was negative for higher

FIG. 4. Bronchography taken on January 19, 1937 showing bronchiectasis of the right lower lobe with cavitation of the right middle lobe.

bacteria.   From January 8 to January 11, 1937, the patient's temperature ranged between 99.6° and 101.6°F., and then returned to normal. On January 11, 1937, roengten examination of the lungs showed "a considerable degree of resolution of the process of the right middle lobe." Dr. Rabin reported this region to be "honeycombed" and the site of bronchiectatic disease.   The pleura over the right lower lobe was thickened.   The cough had greatly diminished and the sputum was decreased to about two ounces a day.

A bronchography on January 19, 1937, showed "no evidence of an obstructive lesion in the middle lobe. The oil entered an irregular cavity about one inch in width which was situated in the anterior portion of the middle lobe at the level of the fourth costal interspace anteriorly. There were also sacculated bronchiectases of branches of the anterolateral and posterolateral divisions of the lower lobe bronchus. The branches of the upper lobe appeared normal. The bronchi of the left lung were not outlined by the oil" (Fig. 4). A bronchography was done on January 26, 1937 to determine the condition of the bronchi of the left upper lobe. This showed all the branches of the left lung to be well outlined, and no abnormality was present. At the time of discharge from the hospital, February 2, 1937, the patient was up and about and afebrile. Her cough was very slight and productive of about one-half to one ounce of non-foul sputum daily.

COMMENT

The clinical course of this patient has been most unusual. After a longstanding history of pulmonary disease dating back to an adenoidectomy twenty-five years previously, she presented all the evidences of a putrid lung abscess of the right lower lobe seven and one-half years ago. This cleared up spontaneously, except for some residual interstitial fibrosis in the right lower lobe. Three years later, without obvious cause, she developed a putrid abscess of the left upper lobe. This in turn subsided spontaneously. Then, after a free interval of four years, she developed a putrid abscess of the right middle lobe, which also tends toward spontaneous cure. This lesion, however, bears watching, because there is already a beginning bronchiectasis of the right middle lobe. The bronchiectasis of the right lower lobe is probably of long standing. The production of these recurring putrid infections of the lung may be traced to the chronic bronchiectasis of the right lower lobe as feeding focus. At first glance, this case may be cited as evidence against the operative treatment of abscess of the lung. One should bear in mind, however, first, that this is a most unusual case, and second, that the patient is left with residual disease, namely a chronic bronchiectasis of the right lower lobe and a beginning bronchiectasis of the right middle lobe. Operative intervention, however, at this time is not indicated. Pneumothorax therapy has been considered, and will be given should any symptoms recur.

CHRONIC EPIDEMIC ENCEPHALITIS WITH MASSIVE SCAR FORMATION IN THE MIDBRAIN SIMULATING BRAIN TUMOR

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The existence of chronic epidemic encephalitis was already recognized by V. Economo during the early studies of this disease. His description of the anatomical changes in material available at that time, however, indicated that the alterations were more of the character of a subacute inflammatory lesion with secondary degenerative changes, rather than in the nature of an advanced sclerosing, scar-forming process. During the past fifteen years or more a large array of cases, clinically identified as parkinsonian syndrome, has been recorded as instances of chronic encephalitis. However, the reported histological findings do not include the mesodermal proliferative changes, such as are seen in an outspoken chronic productive lesion, nor the advanced scar-forming reaction, like that found in the following case. The latter, however, removes every doubt as to the possibility of such an occurrence and also demonstrates that such a scar-forming process may advance to such a degree as to acquire the character of a granuloma and provoke signs of an expanding lesion.

CASE REPORT

History (Adm. 368130). The patient, B. I., was a 36 year old man at the time of his admission to The Mount Sinai Hospital. He was said to have been mentally somewhat retarded and emotionally unstable since early boyhood, but otherwise well until three years before entering the hospital. He then suddenly developed transient diplopia, unaccompanied, however, by other manifestations of an acute inflammatory disease of the brain. Six months later he began to experience progressive loss of power in the left arm and leg. This was followed by spasticity of the involved extremities and by a fine tremor of the hands, which was soon changed into coarse, jerky, and, at times, ballistic, violent movements of the left upper extremity. More recently it was noted that his eyes assumed a staring appearance and his face became rigid and expressionless. At the same time salivation and perspiration became profuse. His emotional instability became more pronounced. He began to complain of blurred vision, developed urinary incontinence and frequency, drank and voided excessive amounts of fluid.

Examination. The patient showed prominent breasts, a corpulent abdomen, feminine distribution of fat about his pelvis, hypogenitalism, and an undescended right testicle. Mentally he was quite alert, rather talkative, oversolicitous, and displayed but slight intellectual inadequacy.

The pupils were unequal, the right larger than the left; both reacted normally to light and in accommodation. There was slight horizontal and vertical nystagmus. The fundi showed moderate blurring of the nasal disc margins, more pronounced on the left side, suggesting early papilledema. Supranuclear facial paresis, reduced power in hand grip and hemihypalgesia and hypesthesia were found on the left side. The deep reflexes were active but unequal, the left greater than the right. The abdominal reflexes were absent and a Babinski sign was elicited on the left side. His gait was propulsive, broad-based, spastic and unsteady. He held his left upper extremity in abduction. There was marked ataxia, intention and action tremor in both upper extremities, more pronounced on the left side. The left upper extremity would frequently display coarse, ballistic movements.

Course. The mode of onset and unfolding of the clinical picture and the neurologic findings suggested the diagnosis of a postencephalitic parkinsonian syndrome. However, the disc changes and the roentgenograms of the skull pointed to the existence of an expanding lesion. Subsequent ventriculographic studies revealed immense symmetrical, bilateral expansion of the lateral ventricles without shift and with the third and fourth ventricles poorly outlined. In view of the ventriculographic findings and the advancing papilledema, an exploratory craniotomy in the region of the posterior part of the third ventricle was thought advisable. However, the operation did not disclose a tumor. The patient ceased on the day following the operation.

ANATOMICAL FINDINGS

Gross Anatomy. The brain appeared to be under increased tension; the gyri were flattened. There was a large operative defect in the right supramarginal gyrus and postcentral gyri. The floor of the third ventricle showed a decided bulge. The left posterior clinoid process was entirely eroded; the right broke easily; the floor of the sella turcica was extremely thin.

The brain, when sectioned, disclosed a markedly enlarged ventricular system. The large defect in the right hemisphere noted on the surface was found to extend into the anterior half of the lenticular nucleus. There were also hemorrhages in the thalamus and the lenticular nucleus on the opposite side. A portion of the corpus callosum and a large part of the fornix were disorganized. In the region of the right pulvinar there was a mass of discolored necrotic tissue. It could be traced into the tegmentum of the midbrain. The right half of the midbrain was enlarged; the aque-

Fig. 1. The gross appearance of the midbrain showing the swelling of the right cerebral peduncle and the hemorrhagic area within its tegmentum.
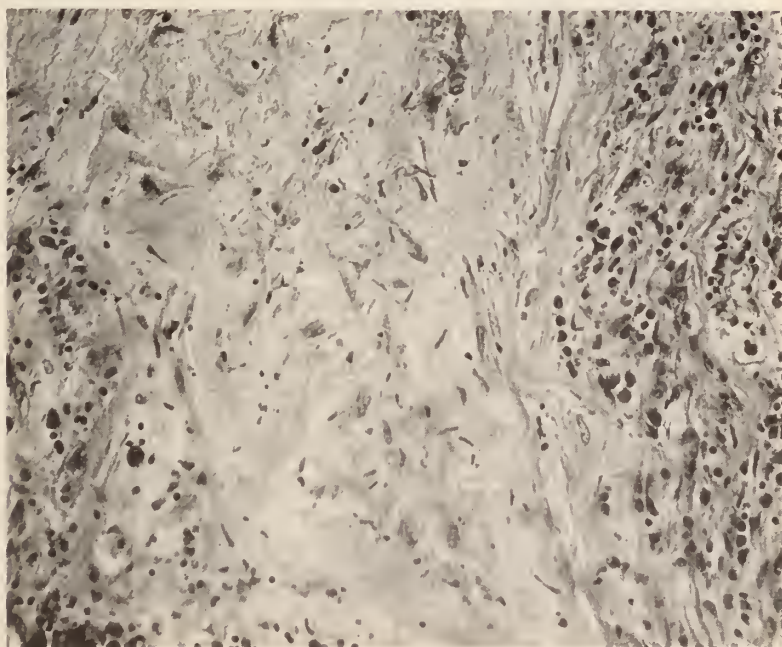
Fig. 2. Scar tissue in the midbrain.

duct was compressed and displaced to the left, and the substantia nigra was almost completely replaced by a reddish hemorrhagic substance (Fig. 1). On tracing this area, it was found that at the end of the midbrain it became continuous with the areas of disorganization in the subthalamus and striatum, while posteriorly it extended into the anterior portion of the tegmentum of the pons on the ipsilateral side. There was also a small area of discoloration in the left half of the tectum of the midbrain.

Microscopic Anatomy. Sections of the midbrain and the hypothalamus revealed all gradations of an inflammatory disease. The most conspicuous lesions were two large circular areas of altered structure in the right tegmentum mesencephali, extending for a short distance into the ipsilateral
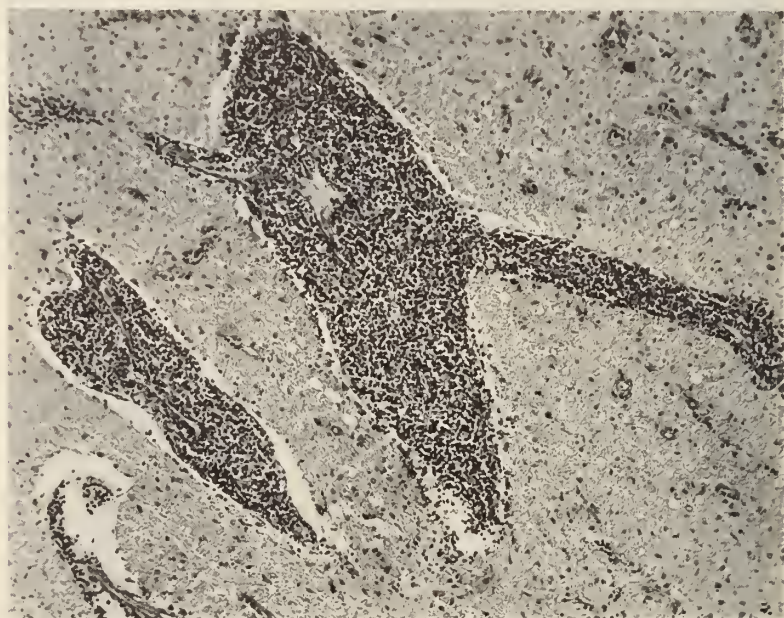
Fig. 3. Perivascular infiltrations peripheral to the scar tissue.

tectum and basis mesencephali. These circular defects were filled with blood elements and surrounded by dense zones of connective tissue (Fig. 2). In between the fibers forming this scar tissue there were large accumulations of pigment-containing macrophages. Immediately outside the wide zone of connective tissue surrounding the hemorrhagic areas, there were numerous vessels, encircled with dense rings of perivascular infiltration (Fig. 3). The infiltrating cells were predominantly small mononuclear elements (Fig. 4). Many of the vessels showed marked thickening of their adventitial coats, others advanced sclerosing and calcifying changes (Fig. 5). Several larger vessels showed necrotic changes, and the size of one was such as to suggest an aneurysmal formation. The zones of vascular proliferation and perivascular infiltration were enveloped by a
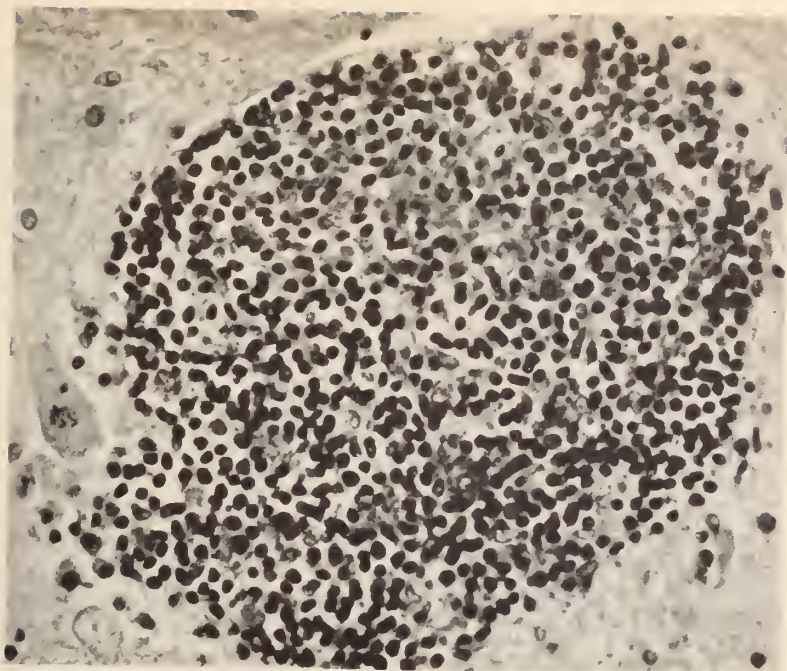
FIG. 4. Areas of infiltration in the region of the nucleus of the oculomotor nerve showing disintegrating nerve cells and the small round cell character of the infiltration.
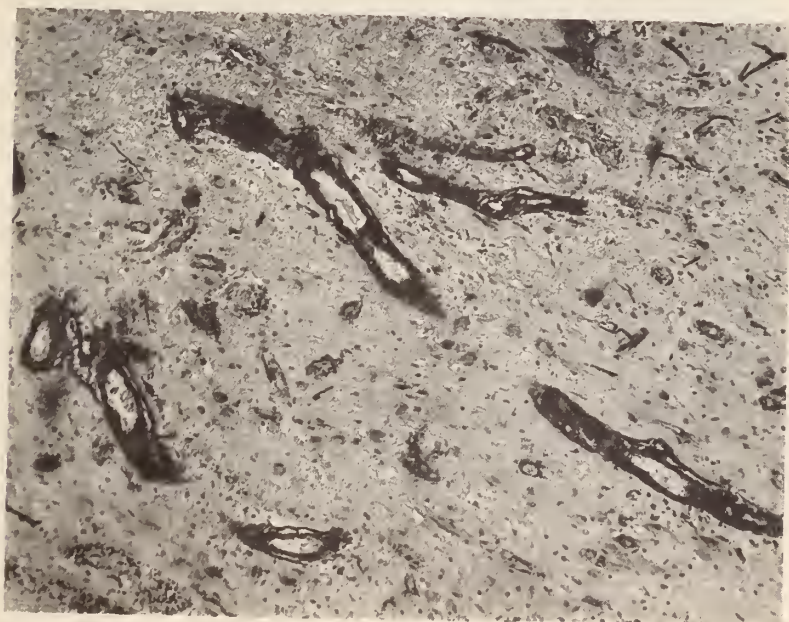
FIG. 5. Vessels in the proximity of the affected area of the midbrain showing degenerative changes.

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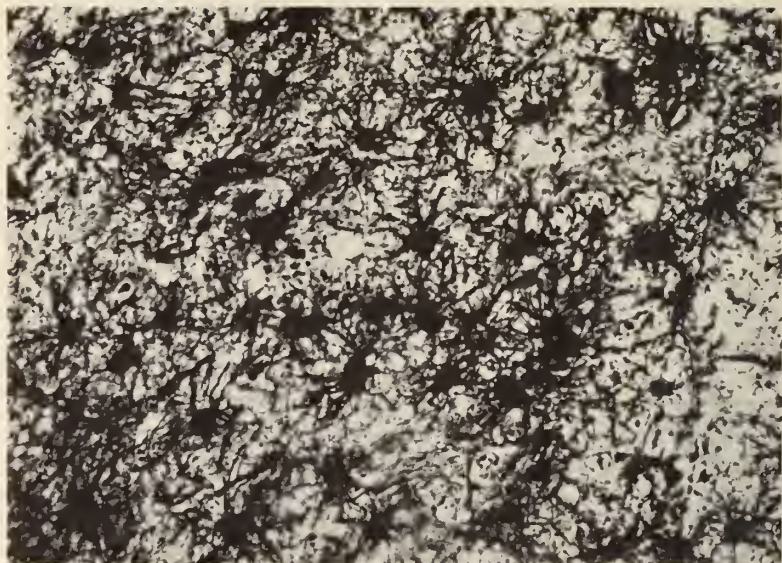
FIG. 6. Gliosis in the midbrain in the zone bordering upon the inflammatory area.
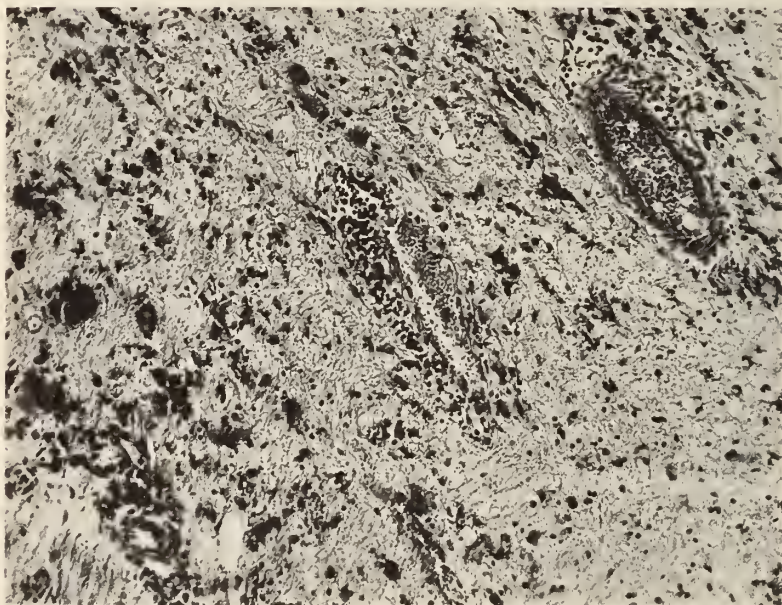
FIG. 7. Substantia nigra showing almost complete loss of pigmented cells. Only a few of them are present and these are very definitely distorted.

belt of dense gliosis (Fig. 6).   Mature astrocytes, some extremely large and swollen, formed a wide band of interlacing fibroblastic glia.

The adjacent substantia nigra had retained its normal structure only in

its median wing on the right side. The cells of the lateral portion had disappeared or were in the process of disintegration (Fig. 7). The pigment liberated by these cells was apparently picked up by macrophages found in large groups in this vicinity (Fig. 8). Iron stains failed to demonstrate iron in the substantia nigra, except for small amounts about blood vessels. The red nucleus on the right side presented moderate degeneration and inflammatory alterations. In the cerebral cortex, distal to the operative field, no outspoken inflammatory lesions could be found. There was, however, considerable ependymal fibrosis and subependymal gliosis.

COMMENT

The anatomical findings, as described above, are almost completely summarized in the title, "chronic encephalitis with massive scar formation
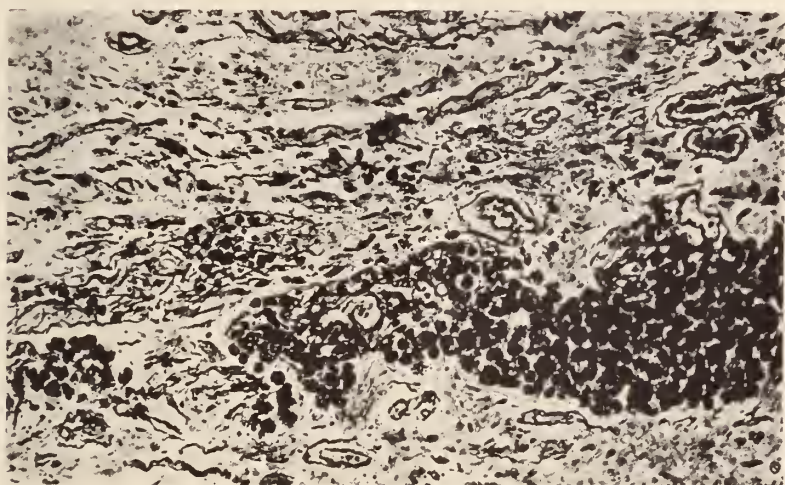
FIG. 8. Collection of macrophages containing large quantities of pigment material probably released by disintegrating cells in the substantia nigra.

in the midbrain and hypothalamus." The large vessel in the center of the disease process is unusual for its location and would tempt one to consider it as an aneurysm. But the fact that its wall is intact and that it is surrounded by a wide zone of inflammatory disease, varying from the acute infiltrative to the advanced chronic sclerosing stage speaks rather in favor of mesencephalitis with secondary alterations in the local vascularization.

The clinical manifestations are readily explained by the character and the location of the lesion. The productive lesions about the aqueduct are, of course, responsible for the obstructive hydrocephalus which resulted in the manifestations of increased intracranial tension. The location of both the subacute and chronic inflammatory process in the midbrain explains fully the parkinsonian features in the case, while the encroachment upon the medial lemniscus by the tegmental scar is the cause of the contralateral sensory disturbance.

NON-SUPPURATIVE THROMBOPHLEBITIS

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Due largely to tenets enunciated by Virchow, opinion in the middle years of the nineteenth century held thrombosis to be the essential and primary lesion in the evolution of the great majority of cases of non-suppurative thrombophlebitis. Inflammation of the vessel wall, when found, was thought to be a secondary effect. This view was tenaciously adhered to, despite the earlier concept of a primary phlebitis introduced by Hunter in 1793 and elaborated by Cruveilhier (1829–1842). "Bland, marantic" thrombi, it was considered, needed only the factors of disturbed, slowed circulation, or alteration in the blood provided by debilitating, emaciating or infectious disease states to cause their formation.

With the advent of bacteriology the order was again reversed. Weigert devised his bacterial stain, and with it found unsuspected bacteria in the walls of vessels of many cases of "bland, marantic" thrombi occurring in fevers, cachectic states, and postoperative convalescence. Widal and others found streptococci in the walls of thrombosed uterine veins in cases of typical milk leg. This form of phlegmasia was thus readily attributed to a primary bacterial phlebitis, the thrombosis occurring secondarily to involvement of the vein wall. At the time of Welch's review of the subject of thrombosis (1898), the pendulum had definitely swung back to a concept of primary vessel wall change as the mechanism in thrombophlebitis, with mechanical and physicochemical factors, such as systemic disease, circulatory disturbance, and blood change, considered merely as contributory factors. Even the non-bacterial cases were now attributed to a primary toxic inflammation of the vein wall.

With manifest disease of the vein wall, or infection or trauma in the vicinity, the mechanism by which a primary phlebitis might occur seemed evident. But in the large group of cases of deep iliac thrombophlebitis, the mechanism was not as clear. It was considered that infection reached the vein wall through the blood stream, and the possible rôle of the lymphatics was ignored. Welch, in his review, stated that the probable mode of entry of the bacteria to the vein wall was through the circulating blood rather than through the vasa vasorum or lymphatics. Since that time considerable evidence has been accumulated to show that the pathway by which infection reaches the vein in deep iliac thrombophlebitis is frequently lymphatic, or that, at any rate, lymphatic involvement primary

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or secondary to the phlebitis contributes significantly to the clinical pic-
ture. Concomitant consideration of the edema, the most conspicuous
feature of deep iliac thrombophlebitis, provides the best approach to this
problem.

The anatomic proximity of the larger lymph vessels to the principal ar-
teries and veins of a limb was first described by Cruikshank in his classical
treatise on the absorbents, published in 1790. He noted, in his painstaking
preparations, that the superficial lymphatics follow the superficial veins;
the deep-seated ones, the arteries. Above the saphenous opening, they
both unite to form two large trunks with numerous intercommunications
grouped in and about the arteriovenous sheath.

Wyer in 1808 described five cases of phlegmasia alba dolens in a paper
entitled "Observations on the *Lymphatic Distention** of the Lower Ex-
tremities of Women While in the Puerperal State." One case, following
promonitory symptoms of heaviness and weariness in the leg and thigh,
developed first swollen and tender inguinal glands, then pain descending
along the course of the lymphatics to the knee, and then to the toes, accom-
panied by marked constitutional symptoms. Only after the progress of
the pain did edema set in, descending from the thigh. He also noted on
the side of the tibialis anticus a tender red streak extending from the top of
the foot to the knee. The tenderness was particularly marked below the
middle of the muscle at the site of a large lymph gland. When restitution
finally occurred and the patient was permitted out of bed, there re-
appeared, after she had walked a short distance, not only swelling and
tenderness, but the red streak on the anterior surface of the leg. Wyer
concluded that the disease depended upon the accumulation of lymph in
the leg, this accumulation depending upon causes peculiarly connected
with the puerperal state.

Cruveilhier, though he did not appreciate the implications of lymphatic
involvement, observed in his cases of thrombosed iliac veins, the inflam-
matory process always in the tissue surrounding the veins and never in
their lining.

Matas in 1913 discussed the effect of repeated cutaneous infection on
lymph stasis and permanent elephantoid states. He recognized that non-
tropical elephantoid lymph stasis might follow phlebitis upon which was
superimposed repeated attacks of lymphangitis.

Halstead and Reichert, and later, Reichert alone, in work first reported
in 1921 and amplified since, showed by sectioning all the tissues of a dog's
leg except the main artery and vein that edema appeared and disappeared
coincidentally with the regeneration of lymphatics across the line of in-
cision. Section of the artery and vein after this regeneration had occurred
caused only a transitory edema while blocking of the regenerated lym-

* Italics mine.

phatics by injection of india ink particles caused a more extensive and permanent edema.

Homans, interested specifically in determining an interrelationship between thrombophlebitis and lymphatic obstruction, ligated common iliac, external iliac, and femoral veins without the production of edema. By injecting muscle juice, ferric chloride, or streptococcus viridans into an isolated segment of femoral vein, he obtained a quite typical edema. The resulting reaction was primarily perivenous. The clot was adherent only at the point of ligature, indicating that the vein wall was little injured even though the material had been injected into the vein lumen. By stripping the sheath from the femoral artery and vein for an inch, and loosely entwining gauze around them, edema extending from the thigh to the knee resulted. Clinically, he observed active exudative processes about both the great vessels within the arteriovenous sheath at the brim of the pelvis in most cases of phlegmasia. Also, the most active seat of the disease was above the inguinal ligament, the disease dying out in intensity as it approached the knee. Concluding that confinement and compression of the principal lymphatic trunks within the inflamed arteriovenous sheath was the main cause of the edema, he decompressed the external iliac sheath (with considerable technical difficulty because of the brawny vascular exudate) in an early case of phlegmasia with an extremely satisfactory result. Another patient, with more chronic, though less severe, disease was treated similarly. Here the results were not quite as satisfactory objectively. This he attributed to the duration of the disease which had converted the sheath into a nearly solid scar. He also cited a case of phlegmasia which was clearly of lymphatic origin. A subcutaneous infusion was given in the outer part of the thigh which left a residual, small, tender lump at the site of infusion. In ten days there followed slight, tender swelling of the femoral and lower iliac nodes. Simultaneously moderately severe pain was experienced in the right thigh and twenty-four hours later there appeared moderate edema of the entire limb.

Leriche produced experimentally a severe perivenous reaction by injecting sclerosing solutions into the adventitia of the main venous trunks of the lower extremities. An extensive edema usually ensued. Though he invoked a different mechanism to explain the production of the edema, that of involvement of the vasomotor nerves by the perivenous reaction, he did conclude that the venous occlusion had little to do with the production of the edema and that the perivenous reaction was the all important factor.

Confirmatory evidence is offered by the diminution of arterial pulse frequently observed early in the course of the disease, by the contraction of the artery seen in early exploration, and by the shrunken spastic artery found in later cases (the second case explored by Homans, referred to above). Since both the artery and vein are included in a common sheath,

one would not expect the artery to be spared if the inflammatory process were primarily in the perivascular sheath. The initial pain of milk leg may very well be due to an ischemia of arterial origin.

In the light of the accumulated evidence it is easy to understand the growing tendency to ascribe to lymphatic obstruction the essential rôle in the production of the edema. However, some degree of venous obstruction is usually manifest; thrombosis is, of course, a constant feature, some cyanosis is usually present; and though mild to moderate dilatation of collaterals would be masked by the extensive edema, not infrequently extensive anastomotic channels between the veins of the thigh and of the abdominal wall attain prominence. It would be unnatural were there not a school attributing edema to venous obstruction. An impetus has recently been given to this line of thought by observations of Zimmerman and de Takats.

These investigators repeated various ligations of the iliac and femoral veins, their collaterals and contralateral veins in all possible combinations, without the production of edema. They then produced a localized chemical phlebitis and periphlebitis by the injection of 50 per cent sodium salicylate into an isolated vein segment without resultant edema. Removal of the iliac lymph glands and the retroperitoneal fatty and areolar tissue from the bifurcation of the aorta to Poupart's ligament did not cause edema even with the division of the common and internal iliac veins. An extensive venous thrombosis was then produced by the intravenous injection of 50 per cent to 70 per cent alcohol distal to a femoral vein ligature. Marked edema resulted. To eliminate the perivenous irritation they then used tissue extract from the heart muscle of dogs and the dog's own serum. Again extensive peripheral thrombosis and edema were produced. Despite the edema, india ink injected into the foot pads reached the iliac glands, though its transit was delayed. The writers concluded that though lymphostasis played a rôle, it was secondary in importance to the venous obstruction. However, it does not seem that a lesion was produced comparable to that found clinically. They showed only that widespread peripheral thrombosis without appreciable involvement of the lymphatics could cause edema. It is doubtful whether such a degree of thrombosis ever is seen clinically. The clinical process is slower in its development, and even in the most extensive thromboses, canalization or collateral channels, adequate to care for the venous return, develop, with edema often persisting long after. The pathological findings likewise differed from those seen in explored cases or in the experimental work of Homans and of Leriche. No active exudative process was found about the vessels, which also explains the patency of the lymphatics to india ink. Moreover, though the edema fluid was high in protein content, it differed from that found in cases of phlegmasia by its hemorrhagic nature. Though Zimmerman and de Takats were unsuccessful in producing edema

by injecting irritants into isolated vein segments or by lymphatic stripping, Homans and Leriche were able to do so. It would have been interesting had an attempt been made in these cases to determine the integrity of the lymphatics by india ink injections.

So far the discussion has been focused particularly on the phlegmasia alba dolens type of thrombophlebitis. Other varieties, of course, exist. The most satisfactory division for clinical purposes is that of Homans. He divides non-suppurative thrombophlebitis into those forms occurring in varicose veins and those occurring in previously normal veins. The latter group he in turn subdivides into phlegmasia alba dolens, phlebitis migrans, superficial thrombophlebitis, and thrombosis of the deep veins of the leg due to local injury or infection. No classification in so complex a field can hope to be universally applicable. There is undoubtedly overlapping between groups, and frequently, ill-fitting or border line cases are encountered.

The varieties other than phlegmasia alba dolens need not occupy much of our time since their pathogenesis is usually obvious. In varicose veins there is outspoken vein wall disease with latent infection often residing therein (de Takats). Phlebitis migrans is essentially a disease of the vein wall with thrombosis incidental. Superficial thrombophlebitis, other than that due to direct trauma or to infection of the vein, as in intravenous injections, or that due to local infection in the vicinity, is uncommon. Occasionally it does occur in serious infections or fevers, rarely following childbirth. Thrombosis of the deep veins of the leg due to local injury or infection is an unusual condition, best elucidated by Homans' own description: "Occasionally, and from seemingly trivial causes, such as fracture of a metatarsal bone, or trifling infection of the leg, thrombosis occurs in the great veins within the muscular aponeurosis of the calf. The cyanosis and swelling which result are confined to the leg and foot, subsiding rapidly upon rest in bed and recurring when the individual attempts to get about. The disease is apt to be long drawn out and is likely to end in a fatal pulmonary embolism. It can be distinguished from phlegmasia alba dolens by the greater blueness which it gives to the foot and by the absence of massive edema of the entire leg.

"The peculiarity of the thrombosis which makes it so very dangerous is the tendency for the thrombosing process, having occupied much of the great network of vessels among the muscles, to spread to the main channels, that is, the popliteal and femoral veins, in the form of a long loose clot, adherent only at its origin, causing no actual obstruction and waving freely in the current, ready to break off with a fatal result. The writer has seen this happen twice in a series of four cases. In one instance the condition vacillated between activity and apparent cure for months; in another, the embolism occurred within ten days of the first symptoms. Unfortunately the disease is remarkably deceptive. Though there may be some

local heat, there is little or no tenderness in the calf or popliteal space. After a few days in bed, the leg (the superficial veins being intact and most of the femoral channels being unobstructed) regains an almost completely normal appearance. It would seem, then, as if healing might well occur without the formation of the loose clot in the femoral current, and doubtless in some instances this actually happens. Yet, of the two cases of this kind which the writer has seen recover, one was subjected by him to ligation of the femoral vein in Hunter's canal."

It is noteworthy that in the varicose vein and superficial varieties considerable reaction is often observed in the tissues adjacent to the vein involved, indicating that primarily or secondarily perivenous inflammation with implication of the lymphatics draining the local area plays a rôle.

In phlegmasia alba dolens, the pathway of vein involvement is probably through the lymphatics draining the pelvis or legs. It is also conceivable that the organism or toxin may reach the vein through the blood stream via the vasa vasorum or the intima, setting up, despite this avenue, the major inflammatory process in the perivenous region. That this can occur has been shown in the experimental work already cited.

To primary or secondary lesions in or about the vessel wall, then, are accorded the essential pathogenetic significance in the production of thrombophlebitis. In accordance with the evidence, edema in thrombophlebitis is attributable to lymphatic obstruction produced by inflammatory involvement or mechanical obstruction within the inflamed arteriovenous sheath of the main lymphatic trunks draining a given area. The perivenous process may precede or follow inflammation of the vein itself. Venous thrombosis and obstruction occur secondarily and are usually in the background.

Thus far there has been omitted consideration of a very important form of thrombophlebitis, the type revealing itself not by local signs, but by pulmonary embolus. Bancroft and his co-workers calculated a blood-clotting index from prothrombin, fibrinogen, antithrombin, blood platelet, and degree of platelet lysis determinations. On the basis of their findings they offered evidence for the existence of a "biochemical" increased clotting tendency which, in addition to the other factors commonly considered (stasis, trauma, infection, and dehydration), facilitated thrombosis. Eleven cases of thrombosis, phlebitis, or embolism studied in this manner were briefly reviewed. All of these had high clotting indices. By further studies they also found that the clotting index could be altered by appropriate diet. Phlebitis, they felt, apart from the septic type and phlebitis migrans, should be divided into two groups: (1) phlebitis and periphlebitis in which clinical symptomatology referable to the vein is prominent and embolization infrequent, and (2) thrombophlebitis with thrombosis the predominating feature. The latter is frequently unrecognized clinically, embolization often being the first phenomenon calling the possibility of its ex-

istence to attention. Most authors segregate a similar group which they designate "thrombosis" in contradistinction to clinically manifest phlebitis.

Such a division offers attractive theoretical possibilities. Embolism is unusual in phlegmasia alba dolens or in any of the other forms of phlebitis, mentioned above. With good clinical evidence of inflammation of veins thrombi are not likely to be dislodged, clinically recognizable thrombosis antedating major embolism only in exceptional cases (Barker, Zimmerman). The segregation of this group would help to clarify why this is so. Thrombi arising secondarily to vein wall inflammation we would expect to be firmly incorporated in the inflammatory process. Were there a group in which thrombosis were primary, it would well account for the absence of clinical symptoms and the non-adherent nature of the clot. However, cases occur in which no such clean-cut partitioning can be made. It may be that the apparent distinction is one of degree, depending on the size of the initial lesion, with propagation of a disproportionately large thrombus from a minimal primary vein wall insult. Whether we are justified in separating off a qualitatively distinct group could possibly be ascertained by appropriate vein wall studies in a large series of cases.

There follows an extremely unusual case of thrombophlebitis in a young man, characterized by obvious clinical phlebitis and periphlebitis, with, nevertheless, the discharge of multiple emboli to the lungs over a period of seven months.

CASE REPORT

History (B. S. Adm. 376963). On February 22, 1935 there was admitted to the surgical service of Dr. Harold Neuhof a thirty-three year old man with the following history. Seven months previously he had traumatized his right shin about six inches below the knee against an automobile bumper. A superficial abrasion resulted which the patient treated himself. Healing occurred slowly over a period of three to four weeks.

Shortly after healing, a painful swelling of the leg in the region of the calf set in. Phlebitis was diagnosed. There were no associated constitutional symptoms. Pain was too severe to permit walking, though the patient did hobble to the lavatory.

Four to five weeks later, when the pain and swelling had almost subsided, there was a sudden onset of severe cutting pain in the right chest and shoulder, aggravated by breathing. There were chilly sensations but no chill, perspiration, temperature to 102°F., mild cough and expectoration of small to moderate amounts of sputum containing fresh blood and small clots. Examination and X-ray studies revealed consolidation of the right lower lobe of the lung with an extensive pleural effusion. The temperature rose to 103°F. with concomitant rises in pulse and respirations

and a marked leukocytosis. The symptoms abated in one week though they did not entirely disappear for about one month. Physical signs disappeared in a few days (communication from physician attending the patient at the time) and simultaneously the temperature, pulse and res-

Photograph of patient taken on March 16, 1937, showing extensive collateral circulation present. Left side shown for comparison

pirations became normal. The chest was clear in an X-ray study taken one month later. Though during this time there were no subjective symptoms referable to the veins of the right leg, the attending physician states that the short saphenous was still tender and somewhat thickened. After

about a month the patient was permitted out of bed.   On leaving the bed, pain was experienced along the inner aspect *of the left thigh*, although there was no recurrence of clinical evidence of phlebitis.   After several days sudden severe pain was experienced in the left lower chest with a repetition of the previous signs and symptoms.   Subsidence occurred in about two weeks.

From that time until his admission to The Mount Sinai Hospital, the patient was bedridden because of frequent recurrences of pain in various parts of the chest accompanied by bloody expectoration, slight fever and general malaise, each attack lasting several weeks.   There also appeared during this period, while still in bed, recurrent attacks of pain and swelling along the posterior aspect of the right leg.   A milder, shorter episode of swelling of the inner aspect of the *left* thigh also occurred.   Between attacks of chest pain there was a mild morning cough with occasional blood-tinged expectoration.

At one time, about two to three weeks before admission, there was a brief episode of dizziness unaccompanied by neurological signs.   At another time the left eye suddenly became "bloodshot".   Throughout the course of the illness considerable gastro-intestinal discomfort and tympanites were complained of.

About ten days before admission, the patient developed pain and tenderness in the right Scarpa's triangle and at about the same time experienced slight pain and a sensation of tightness in the left posterior chest accompanied by bloody expectoration.   The chest symptoms had practically subsided at the time of admission, but the pain and tenderness in Scarpa's triangle persisted.

The illness was not characterized by weight loss or weakness in its course.   Urinalysis was always negative except for slight albuminuria.   There was no previous history of significance, particularly in relation to the extremities; no color changes, sensitivity to temperature changes, pain, previous phlebitides, or intermittent claudication.

Examination.   The patient did not appear ill; he was well developed and well nourished.   Systemic examination, apart from a suggestion of a friction rub at the right posterior lung base, was negative.

There was a well healed scar over the right tibia about six inches below the knee.   A tender, cord-like right great saphenous vein was palpable in Scarpa's triangle joining with the similar cord-like, tender right femoral vein.   The entire extremity was slightly, though definitely, swollen.   The superficial veins of the limb were somewhat engorged, though there was no evidence of phlebitis elsewhere in the extremity.   Neither dorsalis pedis was palpable, but the posterior tibial arteries and a vessel on the lateral aspect of the dorsum of each foot were felt.   The right foot was slightly cooler than the left.   Color returned more slowly than normally on pressure, on moving toes, or on change of position.

Blood pressure was 120 systolic and 94 diastolic. The urinalysis was negative. White blood count on admission was 12,000 with 70 per cent polymorphonuclear leukocytes, 28 per cent lymphocytes, and 2 per cent monocytes. The hemoglobin was 88 per cent (Sahli). The blood smear showed no abnormality. Sputum was negative. The temperature on admission was normal, the pulse rate 80 per minute, the respiratory rate 18 per minute.

Oscillometric Readings:

	Right	Left
Knee	3	3
Calf	$2\frac{1}{2}$	2
Ankle	$1\frac{1}{2}$	$1\frac{1}{2}$
Foot	$\frac{1}{2}$	1

An X-ray examination of the chest the day after admission showed an unusual shadow in the left lower lobe above the diaphragm with the appearance of an area of fibrosis with bleb formation. Just above this was a small dense round shadow immediately beneath the pleura which was thought by the X-ray Department to represent an old infiltrative process or a recent infarction.

The electrocardiogram showed a left ventricular preponderance, the QRS wave of low amplitude in Lead II, T–1 isoelectric, T–4 upright. The interpretation of the electrocardiograph department was: left ventricular hypertrophy and myocardial involvement.

To obviate a possible fatal embolus, ligation of the iliac vein proximal to the site of involvement was decided upon. Accordingly, three days after admission, the great saphenous vein was exposed by Dr. Neuhof at its junction with the femoral. It was white walled and firm, though elastic, as if it contained some fluid blood. The femoral vein was freed to Poupart's ligament. It was found to be encased in a dense, fibrotic, extremely vascular coat, making dissection extremely difficult and bloody. The femoral vein was aspirated several times. Either nothing or only a small amount of blood was obtained. The upper limit of vein change could not be reached through the limits of the incision which was, therefore, extended upward through Poupart's ligament in an effort to reach the disease limit extraperitoneally. Again a thick, very vascular zone had to be traversed, necessitating the ligature of many small vessels and a number of good sized ones. The peritoneum was stripped away for better exposure of the upper limits, but the junction of the external iliac with the internal iliac could not be seen. The fibrovascular tunic covering the external iliac vein was continuous with that overlying the femoral. It could not be determined whether the common iliac had been exposed because of the difficulty in traversing the vascular zone at the upper levels. However, it was evident that the process extended beyond the limits of surgical accessibility as far as an extraperitoneal approach was concerned.

The patient's condition did not permit of the additional surgery which a transperitoneal approach at this time would have necessitated. Therefore, the iliac vein was secured and divided between ligatures. It was obviously thick walled and diseased. After aspiration of the proximal stump was found negative for free bleeding, the proximal ligature was removed. The lumen was found to contain soft, old blood clot, only partly adherent to the intima. As much as possible without undue manipulation was removed. At no time was any free bleeding from the upper stump encountered.

Now, since the limit of disease had not been reached, and since the operative procedure had necessitated considerable manipulation, the danger of embolus which might very well have proved fatal, occurring before the condition of the patient and of the local site would permit another approach, was very real. Accordingly, the following procedure was devised by the operator. A new ligature was applied to the proximal vein stump and ten cubic centimeters of five per cent sodium morrhuate injected slowly into the lumen. It was hoped that the resulting acute chemical endophlebitis would not limit itself to the local site, but, as is often the case in varicose vein injections, traverse the interior of the vein for a considerable distance, with obliteration of the lumen to a point beyond the diseased site. Since no free bleeding had been encountered there seemed to be no danger of releasing the solution into the general circulation.

The remainder of the operation consisted merely of placing a rubber dam against the peritoneum, loosely packing the extraperitoneal space, and closing the skin around the drains. A specimen of the vein and the perivenous tissue was sent to the pathology department for histological study.

Pathological study of the material removed at operation showed the following. As had been observed grossly at operation, the perivenous tissue was markedly thickened and adherent to the vein proper, which was also thickened. This thickening was due essentially to a diffuse inflammatory and extremely well developed proliferative process confined, for the most part, to the adventitia and outer half of the media. The inflammation was mostly low grade, the small round cell being the dominating cellular element, though occasional foci of acute inflammation with polymorphonuclear leukocytes were seen in the outer portion of the media. Blood vessel formation was marked. The inner half of the media and the intima were relatively free of inflammation. A thrombus showing beginning organization was adherent to portions of the intima. The endothelium, where no thrombus was adherent, was natural. No bacteria were found. A small branch artery removed at operation was seen to be without changes. It is well to comment that only one small portion of the vein was studied. While it is likely from the uniformity of the gross findings along the course of the vein observed at operation that this portion was representative, one must realize the possibility that this may not be so.

The postoperative course was quite satisfactory. The temperature reached its maximum of 101.4°F. on the second postoperative day. At this time the hemoglobin was 80 per cent, the red blood count 4,740,000, the white blood count 20,400, and the blood platelets 250,000. Differential count was non-segmented polymorphonuclear leukocytes 21 per cent, segmented ones 61 per cent, eosinophiles 2 per cent, basophiles 2 per cent, lymphocytes 9 per cent, monocytes 5 per cent and reticulocytes 1 per cent. The regenerative index was zero. The blood cells were qualitatively normal. By the fourth postoperative day the temperature was normal and remained so until discharge. The wound secreted a small amount of seropurulent material for a short while, but cleaned up readily and was well healed at the time of discharge.

On the ninth postoperative day, for the first time, dilated collateral veins were observed on the right side of the abdomen and the right lateral lower chest. The patient was quite comfortable throughout his stay and complained of nothing that might suggest further phlebitis or new emboli. Nor were there any findings suggestive of either. With trepidation, the patient was permitted from bed on the twenty-fifth postoperative day. The only occurrence was moderate swelling of *both* lower extremities. On the thirtieth postoperative day, significant symptoms and signs still being absent, the patient was referred back to the care of his private physician.

A careful follow-up has been maintained to date. The swelling of the extremities disappeared gradually over a period of several weeks. All infiltration in the region of the saphenous and femoral veins disappeared shortly. Occasionally, some swelling of the ankle would reappear for a short while on walking and would be accompanied by a mild sense of fatigue in the limb. The collateral vessels evident on discharge continued to develop over a period of more than a year, becoming not only more numerous but dilated and tortuous, and extending to the left side of the body. Slight pain in the wound was occasionally complained of.

Eight months after discharge, in November 1935, the patient was in an automobile accident in which he suffered a small laceration of the right leg below the knee, bruising and ecchymosis of the inner surface of the left leg, and contusions of the flexor surface of the left forearm. There developed, according to a communication from the physician attending him at the time, a mild phlebitis of the veins draining each site of injury. The patient was kept in bed for three months by his physician and, on his advice, has since worn elastic stockings. We did not see him again until three months later. At this time there was no residual evidence of phlebitis and the only complaints were occasional swelling of the leg and some fatigue on walking. There was also experienced a drawing sensation in the legs on walking long distances.

There have been no further phlebitic manifestations since, although

following a blow on the right leg in July 1936, an ulcer developed which required about three months to heal. The collateral circulation reached its peak of development about six months ago, since which time there has been no further progression and possibly some retrogression. Swelling of the leg no longer occurs, though the patient has been wearing elastic stockings which would tend to prevent it. *At no time have there been embolic phenomena.*

The patient was last seen on March 16, 1937. At this time there were no actual symptoms, and there had been none since the healing of the ulcer. Some vague minor complaints, such as an occasional sense of tightness over the wound and pains in the leg when he awoke in the morning and stretched in bed, were ventured by the patient, but there had been no real symptoms referable to the veins or arteries of either extremity or to the chest. The general state of health was excellent, and the patient had returned to work.

On examination, the collateral circulation, though still marked and extending up the abdomen and chest and over to the other side, was possibly somewhat less than previously. There was no edema of either lower extremity. By measurement their circumferences were equal throughout. Color of the limbs was normal. No thickening of the veins was present. As when the patient was first seen, neither dorsalis pedis, but both posterior tibials were palpable. Oscillometric readings showed an increase over those recorded on admission to the hospital.

	Right	Left
Calf	$3\frac{1}{2}$	$4\frac{1}{2}$
Ankle	$1\frac{1}{2}$	$1\frac{1}{2}$

COMMENT

The writer has been able to find no case in the literature strictly comparable to the reported one although the fully developed picture is that of phlegmasia alba dolens, and the case could no doubt be classified as a deep iliac and vena caval thrombophlebitis of unusual origin and development. However, considering the course and development, rather than the static picture at its height, dissimilarities are apparent between the case presented and the "milk leg" group. An occasional case has been referred to in the literature in which ascent of phlebitis from the leg veins to the femoral or deep iliac veins has occurred, but the course described has been a more rapid, continuous one rather than a chronic, intermittent one. Adams, in a discussion of Homans' paper on thrombosis of deep veins of the leg, mentions one such case. This was a varicose saphenous phlebitis which progressed in one day to the femoral vein producing a typical "milk leg." Homans comments that he has also seen such cases. The isolating features here are the deceptive, protracted course with its intervals of quiescence over a period of seven months before the customary

picture of deep iliac thrombophlebitis appeared, and the multiple emboli which occurred despite the exceedingly well marked vein involvement.

It is not out of place at this point to speculate as to the probable course of events in the reported case.   There was definite clinical progression observed from the veins of the right leg to the saphenous vein in the thigh and to the femoral.   However, considerably before the great saphenous vein in the thigh was involved, first pain, then pain and swelling was experienced along the inner aspect of the *left* thigh.   The only explanation that can be offered for this phenomenon is that the perivascular sheath about the inferior vena cava was involved early in the course through the lymphatics, with first the production of pain in the left thigh through arterial spasm, and later, through retrograde extension of the inflammatory process, actual periphlebitic or phlebitic involvement of the left saphenous or femoral vein.   The predominant periphlebitic nature of the process is further attested to by the fact that signs of venous obstruction did not develop spontaneously, but only after division of the iliac vein.   Also, the repeated emboli, the marked perivascular process and loose clot observed at operation, and the histological findings of relatively intact intima and inner half of media offer additional evidence that thrombosis was secondary, although it is perfectly possible that the emboli were discharged from a propagated clot and that histological sections from another portion of the vein might have shown a more marked endophlebitis.   Finally, further evidence that extension to the vena cava, probably through the perivascular lymphatic route, had occurred, lies in the appearance of edema of the left as well as of the right lower extremity upon leaving the bed after the operation, this despite the fact that no clinical evidence of obstruction to the veins of the left lower extremity was at that time present.

Other features of the case worthy of note are the absence of bacteria in the thrombus, vein wall, or perivenous tissue in the specimen removed, and the clinical evidence of a tendency to phlebitis shown in the follow-up history.

SUMMARY

1. A brief review of the literature on non-suppurative thrombophlebitis is given.

2. Report is made of an unusual case of non-suppurative thrombophlebitis of seven months' duration, involving the right great saphenous, femoral, external and common iliac veins, and probably also the vena cava, with numerous pulmonary embolizations during the course of illness.

3. Cessation of embolization followed or coincided with an ingenious surgical effort when attempt to reach the disease limit had failed.   This consisted of injection of sclerosing solution into the vein lumen proximal to a site of ligation and division well within the scope of involvement.

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CLINICAL PATHOLOGICAL CONFERENCES

George Baehr, M.D., and Paul Klemperer, M.D., *presiding*

Wednesday, March 24, 1937

Lymphosareoma of the Stomach: Negative Roentgenology.

(From the Medical Service of Dr. George Baehr and the Surgical Service of
Dr. Richard Lewisohn)

History (Adm. 404670). The patient, a 52 year old Italian laborer, entered the hospital complaining of epigastric pain, anorexia and tarry stools of five weeks' duration. The onset of his complaints began with constant soreness in the epigastrium relieved by food, occasionally radiating to the left breast. During the two weeks prior to his hospitalization, the pain had become more severe and knifelike in character, but still was relieved for periods of fifteen minutes to one-half hour by milk or alkalies. More recently anorexia, nausea and infrequent bouts of vomiting appeared. About five days before his entrance into the hospital he noted tarry stools. His previous history revealed malaria in 1899.

Examination. The patient was a well developed, obese, middle-aged white male, not appearing ill. There were a few crackling râles at both bases. The heart was normal. There was tenderness in the epigastrium. There were no palpable abdominal masses or viscera; no rectal shelf or lymphadenopathy.

Laboratory Data. The blood hemoglobin was 95 per cent, white blood cells 18,700 per cu. mm. with 74 per cent polymorphonuclear leucocytes. The stool guaiac was four plus. Repeated gastro-intestinal series showed no evidence of any organic lesion in the stomach, small intestine or esophagus. A barium enema was not revealing. A Rehfuss test meal showed a normal gastric acidity with blood in each specimen. Urinalysis and blood chemical values were normal.

Course. Despite the negative roentgenograms, it was felt that clinically the patient had a gastric neoplasm and deserved exploration. A laparotomy was therefore performed under general anesthesia. A saddle-shaped infiltrating neoplasm was found on the lesser curvature of the stomach which extended from a point about two inches above the pylorus to the cardia. In view of its extensiveness the lesion was considered inoperable and the abdomen was closed without drainage.

The patient reacted very poorly following operation. He developed twitchings of his extremities and died with hyperpyrexia forty-eight hours following operation. Blood chemistry values postoperatively were normal.

Necropsy Findings. There was an extensive lymphosarcoma of the stomach, irregular in outline, measuring 14 by 7 cm. and extending from the anterior wall over the lesser curvature to the posterior wall of the organ. The large distal portion was situated on the posterior wall and reached the greater curvature at a point approximately 6 cm. above the pylorus. The edge of the ulcer was well

outlined in its lower two-thirds. Here the edge was thick, protuberant and white; more proximally it lay only 1 mm. above the base. The floor of the ulcer was irregularly craggy and nodular and the wall of the stomach through the affected area diffusely involved. There was also evidence of an acute necrotizing inflammation of the cardia and lower third of the esophagus. Except for moderate enlargement of the lymph nodes along the lesser gastric curvature, the lymph nodes

Fig. 1. Ulcerating lymphosarcoma of stomach and acute necrotizing gastritis and esophagitis.

showed no abnormalities. There were also pulmonary emphysema, edema and congestion. Dr. Klemperer remarked upon the relative infrequency of such tumors of the stomach and pointed out that, of the 590 malignant tumors of the stomach which came under observation at this hospital during the last twenty-five years, only twenty-five instances of lymphosarcoma of the stomach were encountered—an incidence of 4.2 per cent.

Wednesday, March 31, 1937

Lymphosarcomatosis with Involvement of the Heart

(From the Service of Dr. Bela Schick)

History (Adm. 402260).   An eight year old white male was admitted on December 13, 1936 with a history of anorexia, pallor, loss of weight for the preceding six months and a more recent onset of profound weakness, dyspnea and marked vomiting.   Two weeks before admission a biopsy of a cervical gland at another hospital revealed the presence of a lymphoblastoma.

Examination.   The boy was markedly cachectic, experiencing inspiratory and expiratory difficulty.   Several small shotty glands were palpable in the right cervical region, left axilla and bilaterally in the inguinal areas.   One area of mediastinal dulness was increased, particularly on the right side.   The splenic
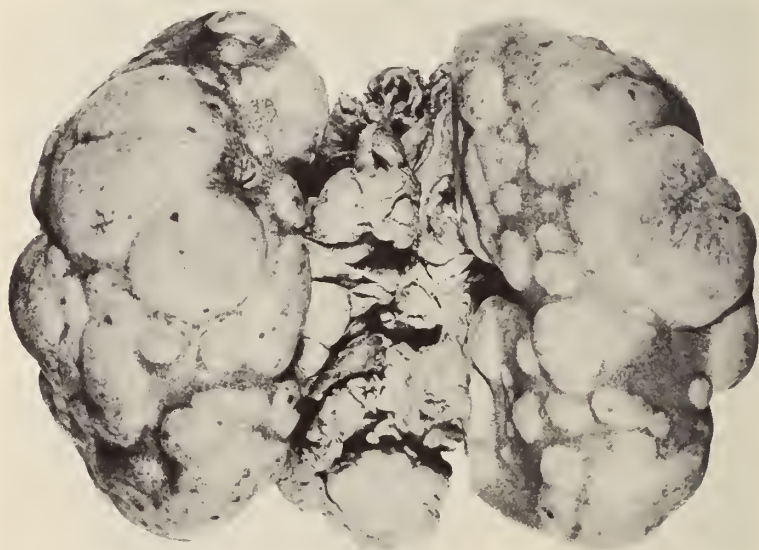
Fig. 1. Massive involvement of kidney in lymphosarcomatosis.

edge was palpable 6 cm. below the costal margin.   There were dulness, diminished breath sounds and occasional râles in the right chest posteriorly; the left was hyperresonant.   The liver edge was at a point 4 cm. below the costal margin; it was firm in consistency.   The cardiac apex was situated in the fifth intercostal space in the anterior axillary line.   The cardiac rhythm was regular and the rate was 136 per minute.

Laboratory Data.   The blood hemoglobin was 90 per cent; erythrocytes 5,500,000; white blood cells 6,000 per cu. mm. with 60 per cent polymorphonuclear leucocytes, 15 per cent lymphocytes.   The red bood cells showed a moderate degree of anisocytosis and very slight poikilocytosis.   Urinalysis was negative.   A roentgenogram of the chest on admission showed marked enlargement of the mediastinal

lymph nodes, particularly toward the right, and a right hydropneumothorax. The blood Wassermann, Schick and Mantoux reactions were negative.

Course. X-ray therapy was instituted soon after admission. It resulted in rapid relief of the respiratory symptoms in spite of an increase in the amount of fluid in the right pleural cavity. During the following thirteen weeks of his hospitalization the patient received several courses of X-ray therapy. Repeated pleural aspirations also afforded relief. The fluid removed was occasionally blood tinged and on one occasion contained a large number of lymphocytes, the morphology of which was suggestive of lymphosarcoma. Reexamination of the chest on January 27, 1937 showed a small amount of fluid at the right base. Also noted was a marked enlargement of the cardiac shadow, particularly to the left. The
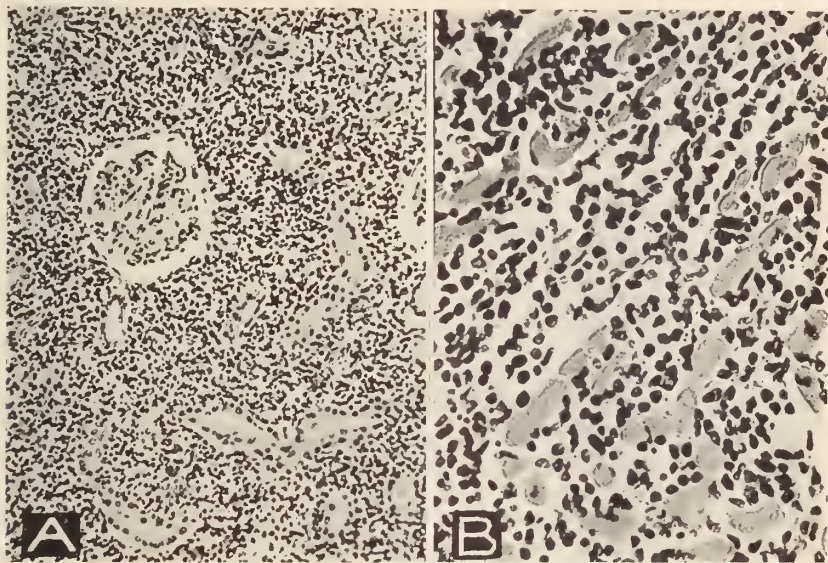
Fig. 2. Lymphosarcomatosis. A. Kidney showing diffuse infiltration of cortex. B. Myocardium with diffuse infiltration.

globular shape of the organ suggested the possibility of a pericardial effusion. However, pulsations were noted fluoroscopically and there was no material change in shape upon variation of the patient's position. The enlarged cardiac shadow persisted throughout his stay at the hospital. The cervical lymph nodes enlarged to a moderate degree. The liver and spleen edges came to a point three fingers' breadth below the costal margin.

In view of the child's marked clinical improvement and relative comfort he was discharged to his home to await an opening at an institution for the chronically ill. The course throughout his stay was only occasionally subfebrile.

Second Admission. The patient was readmitted one day following his discharge complaining of dyspnea. The physical signs were unchanged from those observed on discharge except for a slight increase in the size of the liver and a slight increase in the size of the left supraclavicular lymph node which now was approximately

the size of a golf ball. Dulness was elicited at both bases below the scapular angles. It was suggested that the dyspnea was not due to reaccumulation of pleural fluid alone, but also to circulatory failure, perhaps due to an adherent pericardium, neoplastic in etiology, or perhaps to rapid increase in the size of the mediastinal lymph nodes.

Potain aspiration of the right chest yielded 450 c.c. of a turbid red-yellow fluid and on the left 350 c.c. of a similar fluid. The child nevertheless continued to go steadily downhill and died nine days following his second admission.

Necropsy Findings. There was a generalized lymphosarcomatosis with involvement of the cervical, mediastinal, tracheobronchial, and mesenteric lymph nodes, kidneys, adrenals and testes. A very remarkable feature was a diffuse infiltration of the myocardium, and the pericardial leaflets. An extensive lymphosarcomatous infiltration of the perinephric, posterior mediastinal, retroperitoneal tissues and diaphragm was also found. The right auricular appendage was the seat of a large, partially organized thrombus, and subsequent to this was noted a hemorrhagic infarct of the left lower lobe of the lung. There were also a terminal purulent pericarditis and bronchopneumonia.

Wednesday, April 14, 1937

Case 1. Malignant Hypertension: The Accelerated Phase of Primary Arterial Hypertension.

(From the Medical Service of Dr. B. S. Oppenheimer)

History (Adm. 405044). The patient, a white female of 40, entered the hospital with a history of arterial hypertension of sixteen months' duration. The onset occurred with transitory blindness of the right eye subsequent to an emotional episode. Her systolic blood pressure was found to be 295 mm. of mercury. During the year prior to hospitalization she experienced bouts of severe post-exertional substernal pain which radiated down the left arm. Two months before admission she developed paroxysmal nocturnal dyspnea, and transient amblyopia. Two weeks prior to her entrance, progressive edema of the ankles and oliguria appeared associated with pain across the lumbar spine.

Examination. The patient was an acutely and chronically ill-appearing dyspneic female. The left pupil was slightly larger than the right and responded to light but not to accommodation. The right optic disc was hyperemic; its margins were obscured by a grey exudate which was somewhat elevated nasally. The arteries were markedly reduced in calibre, occasionally to the point of complete obliteration; the veins were dark, irregular and full. Scattered about the posterior pole were small foci of yellow exudate and a diffuse sprinkling of small hemorrhages. The left disc was replaced by a coloboma, with associated myopic degenerative changes.

A slight degree of dulness was elicited at each base, with diminished breath sounds and fremitus and many fine moist râles. The cardiac apex was percussed at a point in the sixth intercostal space 1 cm. to the left of the midclavicular line. The aortic second sound was louder than the pulmonic second and of a bell-like quality. The rhythm was regular. A slow gallop was audible toward the base. There were no murmurs. The liver edge was palpable at a point $2\frac{1}{2}$ fingers' breadth below the costal margin. There was moderate edema of the legs and sacrum The neurological status, except for slight hyperreflexia, was not remarkable.

Laboratory Data. The blood pressure was 270 mm. of mercury systolic and 160 diastolic. The hemoglobin was 78 per cent. There were 21,200 white blood cells per cu. mm. with 82 per cent polymorphonuclear leucocytes, 14 per cent lymphocytes and 4 per cent monocytes. The blood Wassermann reaction was negative. The blood urea nitrogen was 12 mgm; sugar 85 mgm. per 100 c.c. The venous pressure was 12 cm. Urinalysis revealed occasional red blood cells and white cells, and low fixation of specific gravity. A teleoroentgenogram showed marked cardiac enlargement, particularly of the left ventricle and a moderate degree of dilatation of the arch. The electrocardiogram showed left ventricular preponderance and changes indicative of myocardial damage.

Course. For a time the patient showed improvement on bed rest, sedatives and digitalis. Nine days following admission, however, she suddenly developed increased respiratory difficulty. On the morning of her death, two days later, she experienced severe abdominal pain, an exaggeration of dyspnea and orthopnea and died ten minutes later.

The clinical diagnosis considered was malignant phase of essential hypertension, while death was attributed to acute cardiac failure.

Necropsy Findings. Post mortem examination disclosed widespread vascular involvement of many organs which consisted of severe intimal proliferation of the medium and smaller sized arteries, arteriolar hyalinization, and a rare instance of arteriolar necrosis within the kidney. The heart showed a moderate degree of hypertrophy and evidence of recent dilatation. There were also arteriosclerosis of the coronary arteries with narrowing, generalized anasarca, and acute passive congestion of the liver, spleen, kidneys, and gastro-intestinal tract.

Dr. Klemperer emphasized the point that the degree of renal damage was insignificant when compared to the extent and degree of the generalized vascular involvement. The striking feature of the vascular lesion was a cellular intimal proliferation which he designated as "accelerated arteriosclerosis."

Case 2. Malignant Hypertension

(From the Medical Service of Dr. B. S. Oppenheimer)

History (Adm. 406010). The patient, a 44 year old male, entered the hospital with a history of severe headaches associated with intense photophobia in 1922. These complaints lasted for a period of three weeks and then completely subsided. In 1932 he again began to suffer severe right-sided headache which lasted from one-half to several hours. During the presence of the pain he had scotomata of both eyes and distinct impairment of visual acuity. Occasionally there would be an associated complete left-sided numbness and weakness. His blood pressure at that time was within normal limits. Three weeks before the present admission to The Mount Sinai Hospital the patient experienced a sudden onset of oppressive throbbing precordial pain which radiated into the neck. This pain steadily increased both in frequency and severity. Ten days before hospitalization he suffered an attack of paroxysmal dyspnea which had since recurred, and four days before entrance to the hospital he noted increasing impairment of vision. On the day prior to admission he developed sharp aching pain in the right flank and voided a bloody urine.

Examination. The patient was a well developed, well nourished, pallid male. The pupils were contracted; the right was larger than the left, slightly irregular and

reacted sluggishly. The fundi showed marked papilledema, many striate and flame-shaped hemorrhages and scattered areas of exudate. The retinal arteries were extremely narrowed, irregular in calibre. The veins were tortuous and, markedly constricted by the arteries. The lungs, except for fine basal moist râles, showed no abnormalities. The heart was enlarged to the left and downward. The apex was percussed to a point just inside the midclavicular line in the sixth interspace. The aortic second sound was greater than the pulmonic second and reduplicated. A soft systolic murmur was heard at the apical and aortic areas. The rhythm was regular. There was moderate peripheral sclerosis. The liver edge was palpable at the costal margin. There was moderate right costovertebral tenderness. A neurological examination was negative.

Laboratory Data. The blood pressure was 280 systolic and 180 diastolic. The hemoglobin was 70 per cent, white blood cells 13,110 per cu. mm. with a normal differential. The erythrocytes numbered 4,200,000 per cu. mm. The blood urea nitrogen was 60 mgm., glucose 120 mgm.; creatinin 7 mgm., chorides 480 mgm. and cholesterol 470 mgm., calcium 9.4, phosphorus 5.0 mgm. per 100 c.c. The total protein was 7.3 per cent. An electrocardiogram revealed evidence of left ventricular preponderance and a myocardial abnormality. A spinal tap showed an initial pressure of 355 mm. and no evidence of block. Five hours later following intravenous administration of 200 c.c. of 25 per cent sucrose, a spinal tap showed a decrease of initial pressure to 260 mm. The urine showed poor variability of specific gravity with a tendency toward low fixation. There was a moderate degree of albuminuria and marked hematuria.

Course. The patient's course was progressively downhill. The azotemia steadily increased and the drowsiness became more and more marked. On the fourth day after admission he lapsed into coma and died. The kidneys at necropsy showed the characteristic findings of malignant nephrosclerosis. The right kidney in addition contained within its pelvis several small irregular calculi. The heart presented a rather marked degree of hypertrophy (weight, 635 grams) and moderate dilatation of all its chambers. There were also acute thrombosis of the main right circumflex artery, and its posterior right ventricular branch and severe arteriosclerotic thickening of the walls of the coronary arteries with narrowing of the lumina. The myocardium was the seat of scattered foci of degeneration. There were marked pulmonary congestion and edema, acute congestion of the spleen and intestines and bilateral submucosal hemorrhages of the renal pelvis.

Comment. In contrast to the previous case, the cause of death was here ascribed to coronary thrombosis and renal insufficiency incident to extensive arteriolar disease. Dr. Klemperer stressed the fact that the vascular picture of essential hypertension, either of the so-called benign type or the malignant variety, was not confined to the kidneys alone but was also evident in all parts of the body, especially the pancreas and adrenals. In this regard Dr. Baehr pointed out that the clinical manifestations of the disease depend upon the site and degree of the vascular involvement. Almost a third of the instances of malignant hypertension run their course with predominant central nervous system manifestations, e.g., disorientation, mental deterioration, delirium, etc. These cases develop renal azotemia only terminally.

Dr. Oppenheimer questioned the advisability of the use of the terms malignant hypertension and malignant nephrosclerosis. He also emphasized the fact that headache is an early and persistent symptom in this variety of hypertension. Dr. Klemperer was in full accord with such a contention and offered the opinion that the clinical picture should be designated "malignant hypertension" and the anatomical picture "accelerated arteriosclerosis." Dr. Bachr then called attention to the fact that in many cases the accelerated vascular disease becomes engrafted upon the pathological and clinical manifestation of the so-called essential hypertension (arteriolar sclerosis) which may have existed for ten or more years. For years after the onset of hypertension it is impossible to predict whether the clinical course may ultimately end with the fulminating vascular disease. It is therefore futile to attempt to classify cases of hypertension clinically into benign and malignant varieties or into the red and the white forms, as Volhard has done. When the accelerated arteriosclerosis develops, the clinical picture rapidly changes, the patient develops pallor, the blood pressure mounts to much higher levels, albuminuria becomes intense, red cells appear in the urine, the face becomes puffy, circumpapillary edema and other characteristic retinal changes appear, headache and mental disturbances are conspicuous and renal insufficiency ensues.

Reported by HENRY HORN, M.D.

CLINICAL NEUROPATHOLOGICAL CONFERENCE

Monday, April 26th, 1937

Israel Strauss, M.D., and Joseph H. Globus, M.D., *presiding*

Case 1.   *Tuberculous Meningo-encephalitis.*   Dr. David Beres

History (Adm. 397578).   A 27 year old negro was admitted to the hospital on August 25, 1936 with a history of headache for ten days.   Three months before admission he had had an illness diagnosed as pneumonia with pleurisy, lasting for seven weeks.   No thoracentesis was done.   The headache started ten days before entry, in the left frontotemporal region.   It was at first mild, but increased rapidly in severity.   There had been an episode of unconsciousness one week before and also several periods of delirium and disorientation.   Temperature fluctuated to 102°F.   Two years previously he had an episode of vomiting and epigastric pain which was attributed to a peptic ulcer on the basis of X-ray study.   This yielded promptly to medical treatment.

Examination.   The patient was euphoric.   He had depressed deep reflexes. There was slight nuchal resistance but no other positive findings.   Lumbar tap revealed an initial cerebrospinal fluid pressure of 200 mm. of water which, after 10 c.c. had been withdrawn, fell to 120 mm.   There were 24 cells per cu. mm.; no pellicle formed upon standing, and stain for acid fast organisms was negative.

Course.   A diagnosis of tuberculous meningitis was made, with lues to be excluded.   On the day following admission there appeared a slight Kernig sign on the left side.   The Pandy test of the cerebrospinal fluid was 2 plus.   An X-ray examination of the chest at this time was negative.   In the next few days the patient showed some improvement.   There were only 12 cells per cu. mm. of spinal fluid and the Pandy test was one plus.   His temperature, however, rose to 103°F. and the pulse dropped to 60 per minute.   These findings raised the question of the possibility of a benign lymphocytic meningitis.   But his symptoms again increased in severity, and on August 31 the spinal fluid was found to contain 38 cells.   The sugar content was 40 mgm. per cent; the chlorides, 645 mgm. per cent and the total protein, 80 mgm. per cent.   The diagnostic difficulty presented by this case was due to the presence of marked meningeal signs which were inconsistent with the relatively small number of cells in the spinal fluid.

In the next few days the patient again presented improvement in his clinical condition, returning at one time to perfectly clear mentality.   On September 5 the headaches reappeared.   On November 7 the spinal fluid contained 380 cells with 80 per cent lymphocytes.   The sugar content was 35 mgm. per cent, the chlorides 620 mgm. per cent, the total protein 90 mgm. per cent, and the tryptophane test was negative.   Tubercle bacilli were at this time found in the cerebrospinal fluid.   In the succeeding days there developed slight facial weakness, and inequality of the pupils, with a sluggish reaction to light.   The patient also became increasingly stuporous.   On September 14 an encephalography was done, the

X-ray pictures showing a moderate symmetrical internal hydrocephalus. On September 17 the patient ceased.

Necropsy Findings. Gross Anatomy. General post mortem examination showed a calcified primary complex in the upper lobe of the right lung with dissemination to the lungs, spleen, liver and kidneys. The brain was normal in consistency and, when removed, exhibited on its surface numerous small seed-like masses, none greater than one millimeter in diameter, especially on the right side over the frontal pole and lateral aspect of the temporal lobe. These were
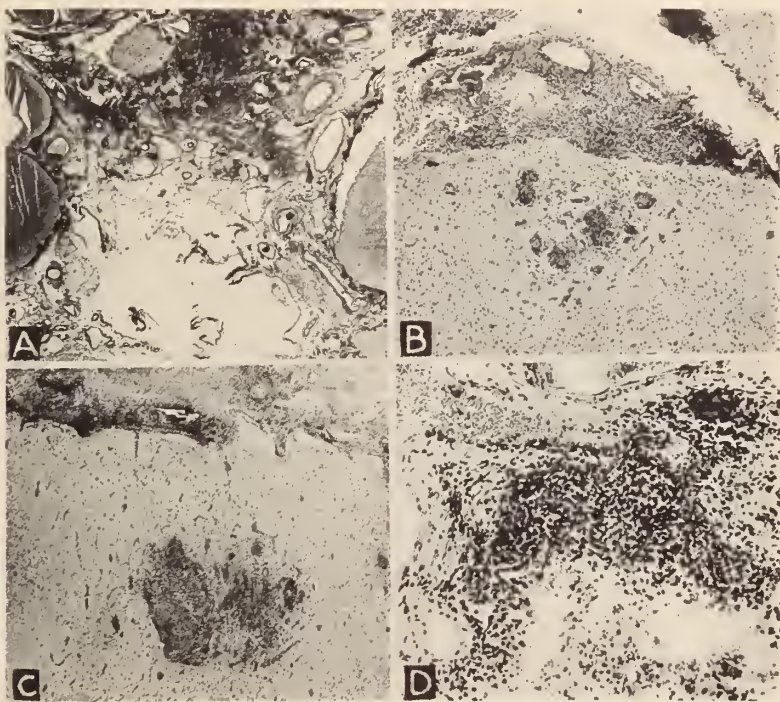
Fig. 1 (Case 1). A. Sections showing serofibrinous and caseous exudate in interpeduncular space (Hematoxylin and eosin stain). B. Section showing perivascular accumulation of lymphocytes in cerebral cortex (Hematoxylin and eosin stain). C. Section showing area of necrobiosis in cerebral cortex (Hematoxylin and eosin stain). D. Section showing area of cellular accumulation in the chorioid plexus (Hematoxylin and eosin stain).

somewhat more numerous along the course of the vessels. At the base there was a thickened, opaque, green-gray-white appearance of the leptomeninx, extending as far as could be seen down the spinal canal. The ventricles were symmetrically and markedly enlarged and their linings were softened and disorganized.

Microscopic Anatomy. Sections showed a dense accumulation of serofibrinous, caseous exudate in the interpeduncular space. The blood vessels showed considerable perivascular, intramural and endothelial cellular infiltrations, consisting mainly of large mononuclear cells and small lymphocytes. Caseation was present. There were no giant cells, although early tubercle formation was evident.

The outstanding pathological features in this case were the marked meningeal exudate with necrosis, and the perivascular infiltrations, especially in the interpeduncular space (Fig. 1 A). Of particular interest was the presence in the cortical tissue of tubercle formations in various stages of development (Fig. 1 B & C). They demonstrated a process in the cortical tissue which apparently was secondary to an extensive meningeal involvement, the spread occurring most probably along the pial extensions around the blood vessels. The presence of normal cortical tissue intervening between the meningeal and cortical lesions favored this interpretation. Serial sectioning of such a lesion would probably bring out at some point a direct connection between the meningeal and the cortical lesion.

The different stages of development of the two lesions illustrated afford some clue to the method of development of such lesions. They seemed to indicate that the spread of the tuberculous process, even from one part of the brain to another, takes place by way of vascular channels.

The chorioid plexus in this case showed areas of small round cell infiltration (Fig. 1 D).

Observations which have been made on a large series of cases of tuberculous meningitis, point to a hematogenous portal of entry of the tubercle bacillus into the central nervous system.

Case 2. Lymphoblastosis of the Meninges. Dr. Mark Kanzer

History (Adm. 383614). A boy, aged 9 years, began to limp and complain o pain in the right knee two months prior to his admission to the hospital. Later, pains and weakness affected both legs so that he had to be confined to bed. During the two months period the child lost ten pounds in weight. A few days before his admission on August 21, 1935 it was noticed that his abdomen was swollen.

Examination. The right lower extremity was maintained in a position of flexion and external rotation; the patient was unable to rotate the limb outward. The right thigh measured 36 cm. in circumference as compared to 30 cm. on the left. The heart was found to be moderately enlarged to the left with a systolic murmur at the apex which was not transmitted to the axilla. The blood pressure was 158 mm. of mercury systolic and 122 mm. of mercury diastolic. There was furunculosis of the scalp and palpable non-tender cervical, axillary and inguinal lymph nodes. The abdomen was markedly distended and palpation revealed a large firm mass on the left which extended from beneath the costal margin to about 3 cm. below the level of the umbilicus and from the flank medially to the nipple line. A second mass was palpated in the right lower quadrant. On rectal examination, a firm tender mass was felt protruding from the right.

There was general diminution of the deep tendon reflexes with absence of the left knee jerk and both ankle jerks. No pathological reflexes were elicited. Fundus examination revealed bilateral pallor of the discs. The right sixth nerve was paralyzed and there was a left facial weakness.

Laboratory Data. Blood examination showed 65 per cent hemoglobin; 3,520,000 red blood cells and 9,200 white blood cells, with 65 per cent segmented polymorphonuclear neutrophiles. Schick, tuberculin and blood Wassermann tests were all negative. Urinalysis revealed two plus albumin, specific gravity 1010, thirty to forty white blood cells (some in clumps) and occasional red blood cells.

Phenolsulphophthalein tests showed 20 per cent excretion in one hour, 30 per cent in two hours. X-ray examination of the pelvis revealed irregular mottling of the right ischium, the cortex of which appeared eroded. An intravenous pyelogram showed a small amount of dye in the left kidney pelvis and some in the calyces. On the right, only a small amount of dye was noted in what may have been the kidney pelvis. The ureters were not outlined.

Course. About a week after admission the patient developed fever of 101–102°F. and symptoms of meningeal irritation. A spinal tap was performed and fluid of ground glass appearance was obtained. Examination revealed 1,350 white blood cells, mostly lymphocytes, and other cells suggestive of the diagnosis of lymphosarcomatous infiltration of the meninges. X-ray examination of the skull was negative. The condition of the patient declined and he ceased two weeks after admission.
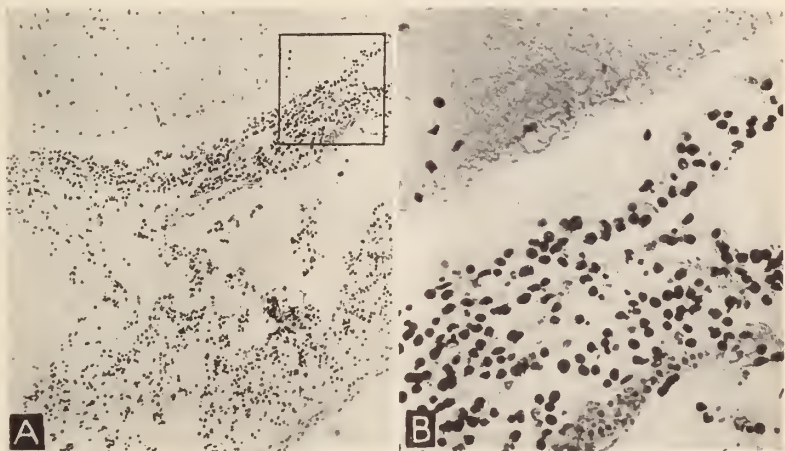
Fig. 2 (Case 2). A. Section showing lymphoblasts in the leptomeninges (Hematoxylin and eosin stain). B. Higher magnification of squared area in A.

Necropsy Findings. Gross Anatomy. A generalized lymphosarcomatosis was found to involve the lymph nodes, visceral organs, pelvic bones and lumbar vertebrae. There were also pulmonary congestion and edema; the left ventricle of the heart had undergone hypertrophy and dilatation, and there were fatty changes in the liver.

The brain and its dural covering revealed no gross pathological changes. Soft, friable material was found adherent to the dura of the lower end of the spinal cord and cauda equina. This tissue could be traced through the intervertebral canals along the spinal nerves.

Microscopic Anatomy. The kidney was found to be the site of the primary tumor. No recognizable parenchyma remained, as it was replaced by tumor tissue. The tumor was composed of densely packed cells which, in scattered areas, formed clumps and clusters. The cells had small round hyperchromatic nuclei surrounded by a thin rim of pinkish cytoplasm and strongly resembled lymphocytes. The stroma was scant and delicate and could be identified usually only in the region of

vessels. Under high magnification, certain variations in the morphology of the tumor cells could be distinguished. While the great majority of the cells appeared like lymphocytes, a number of cells had larger oval or irregular vesicular nuclei with somewhat more cytoplasm. Many of these vesicular nuclei possessed nucleoli. There were numerous delicate intercellular fibers, the nature of which could not be determined, as they might have represented either cell processes or delicate stroma. Mitotic figures were exceptionally numerous, ten and more being counted in one oil immersion field. A section, probably representing the spinal roots, showed thin streamers of these small round cells infiltrating into the walls of the veins. In addition, there were masses of the tumor cells which were metastatic foci. The secondary tumors differed from the primary in that there was greater uniformity in the cell type. Sections through the cord showed small masses of these tumor cells about the periphery. The anterior and posterior roots revealed infiltrations which again followed the connective tissue septa. A section of the cortex (Fig. 2 A & B) showed tumor cells diffusely infiltrating the meninges. The subpial veins were distended with blood and, clotted within the vessels, were clumps of the same cells previously described. They were seen as perivascular infiltrations about the intraparenchymal cortical vessels.

Case 3. Metastatic Carcinoma with Compression Myelopathy. Dr. Mark Kanzer

History (Adm. 385037). A man, aged 36 years, experienced mild pain in the right shoulder and right upper arm eight weeks prior to admission to the hospital. Two weeks later he developed intense shooting pains in the lower dorsal spine which radiated anteriorly to the mid-clavicular line. Three weeks before his admission the patient had a tooth extracted because of an apical infection. One week before admission both legs became numb and heavy and he could not walk without assistance. The numbness spread gradually up to the level of the umbilicus. At about the same time he became increasingly constipated and complained of dribbling of urine and distention of the bladder. Impotence also developed. During this period the patient lost fifteen to twenty pounds in weight. He was admitted to the hospital on September 30, 1935.

Examination. There were numerous scattered nevi over the entire torso of the patient. Localized tenderness was found over the right shoulder and over the seventh dorsal vertebra. He was bed-ridden and there was eversion and flaccid paralysis of both lower limbs, more marked on the left, with diminished deep reflexes in the lower extremities. Power was diminished in the right upper arm but the reflexes in the upper extremities were equal and active. The abdominal reflexes could not be elicited; the left cremasteric was sluggish and the right, absent. The Babinski sign was present bilaterally. Sensation for all superficial modalities was markedly impaired and vibration sense lost below D_8. There was no belt of hyperalgesia. Position sense was completely absent in the toes of the left foot and only partially preserved on the right. Urinary and rectal incontinence were noted.

Laboratory Data. A lumbar puncture showed complete block. Examination of the spinal fluid revealed five cells per cu. mm., all monocytes, and a total protein of 150 mgm. per cent. The colloidal gold reaction was negative. X-ray examination of the shoulder revealed irregular destruction of the outer third of the right clavicle. There was similar destructive involvement of the axillary margin of the

scapula, the paravertebral portion of the seventh right rib and of the right innominate bone.   X-ray examination of the chest showed a circumscribed shadow in the first right intercostal space.   Urine examination was negative, including the tests for Bence-Jones bodies.   The blood hemoglobin was 80 per cent.   Blood and spinal fluid Wassermann tests were negative.

Course.   Soon after admission, tumor tissue appeared at the site of the recently extracted tooth in the left upper jaw.   A biopsy four days after admission revealed embryonal squamous cell carcinoma.   The patient was given a course of intensive
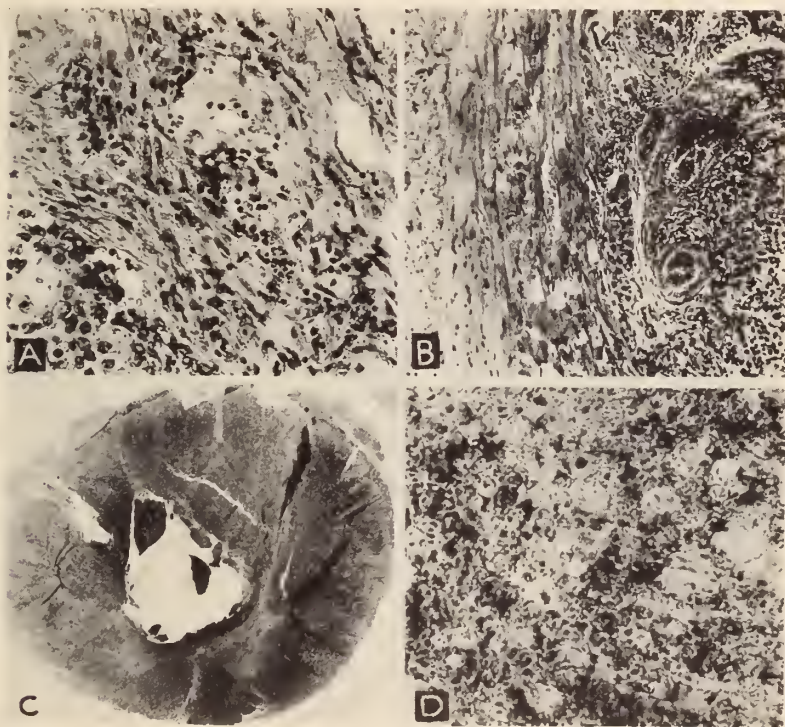
FIG. 3 (Case 3).   A & B. Sections showing infiltration of the dura mater by tumor cells (Hematoxylin and eosin stain).   C. Section of the spinal cord depicting gross destruction of tissue (Marchi stain).   D. Area of myelopathy under higher magnification displaying presence of free fat (Marchi stain).

deep X-ray therapy to the jaw, right shoulder and back, but without producing an improvement in his condition.   The mass in the upper jaw grew rapidly, while within three weeks the signs of a spinal lesion rose to the level of D_1.   Two new masses appeared on the skull.   Terminally, the patient developed bronchopneumonia and ceased five weeks after admission.

Necropsy Findings.   Gross Anatomy.   A primary bronchogenic carcinoma was found in the bronchus of the right upper lobe.   There were multiple osseous metastases including one in the sixth dorsal vertebra compressing the spinal cord. The cervical and mediastinal lymph nodes, lungs, superior vena cava and right

adrenal also showed metastatic growths. The spinal cord revealed massive diffuse softening below the level of compression.

Microscopic Anatomy. Sections of the cord showed infiltration of the dura by nests and columns of large cells with abundant cytoplasm and large, irregular vesicular nuclei with distinct nucleoli and moderate amounts of deep-staining chromatin (Fig. 3 A & B). The cord itself (Fig. 3 C & D) revealed complete dissolution of the cellular architecture (Fig. 3 C) and great numbers of gitter cells at the site of the distintegrating and disappearing parenchyma. Sections stained by the Marchi method showed the presence of degenerated fat products (Fig. 3 D). A few remaining vessels showed moderate thickening.

Comment by Dr. Globus. There is a strong probability that the so-called apical infection, for which the tooth was extracted, was the seat of a metastatic process, as shown by the subsequent rapid growth of a metastatic nodule in that location.

Case 4. Multiple Metastatic Brain Abscesses Associated with Leptomeningitis and Abscesses of the Chorioid Plexus. Dr. Grant Levin

History (Adm. 377870). A 28 year old male entered the hospital on March 19, 1935, complaining of headache and vomiting of four days' duration. He had been well until the age of fourteen when he received a gunshot wound in the left chest, resulting in an empyema. During the next fourteen years he underwent numerous operations for the empyema and bronchopleural fistula with apparent cure at the end of that time (six months prior to admission). Four days before entering the hospital he awoke with a severe throbbing headache and soon after breakfast became nauseated and began to vomit. He was put to bed. He was found to have a fever of 101°F. which was soon accompanied by chilliness and chattering of the teeth. That night he was restless and slept poorly. The next morning the headache was less intense, but he continued to vomit all day and was rather drowsy. On the following day, twenty-four hours before admission, he was unable to move his head because of rigidity of the neck.

Examination. The patient was acutely ill and had a fever of 101°F. There was considerable deformity of the left chest and numerous scars of the previous operations. In the lung field about the scars there were increased vocal fremitus, bronchial breathing and a few râles. The heart was slightly enlarged to the left and auscultation revealed an apical systolic murmur. The liver edge was palpable 3 cm. below the right costal margin. The pupils reacted sluggishly to light, and there was a transient right homonymous quadrantopsia. His neck was markedly rigid, and he exhibited a paresis of the right facial muscles of the mimetic type. Kernig and Brudzinski signs were present bilaterally. There was a general, marked hyperreflexia with the right patellar jerk brisker than the left. The abdominal reflexes were absent and Gordon and Chaddock signs were present on the right side. The Babinski sign was elicited bilaterally but was more marked on the right.

Laboratory Data. The initial pressure of the cerebrospinal fluid was 160 mm. of water; it contained 6,400 cells per cu. mm., 80 per cent of which were polymorphonuclear leucocytes. No organisms were found on a smear.

Course. The patient's temperature rose rapidly to 103°F. and it was felt that, although it was most probable that there was a metastatic brain abscess with secondary meningitis, the possibility of epidemic meningitis could not be excluded.

Therefore, 20 c.c. of antimeningococcus were administered intravenously and 20 c.c. more intrathecally.   Ninety minutes after this therapy (less than twenty-four hours after admission) the patient's temperature rose to 105°F., he became cyanotic and expired.

Necropsy Findings.   Gross Anatomy.   The vessels over the convexity of the brain were engorged and in some instances accompanied by thin lines of yellowish exudate.   The base of the brain, especially about the optic chiasm, was coated by a thin fibrinous exudate.   On separating the medulla from the overlying cerebellum, yellowish pus became visible in the fourth ventricle.   The left temporal lobe was softer than the right and sagged somewhat.   The middle temporal gyrus on the right participated in the formation of a small elevation of bluish hue which, when
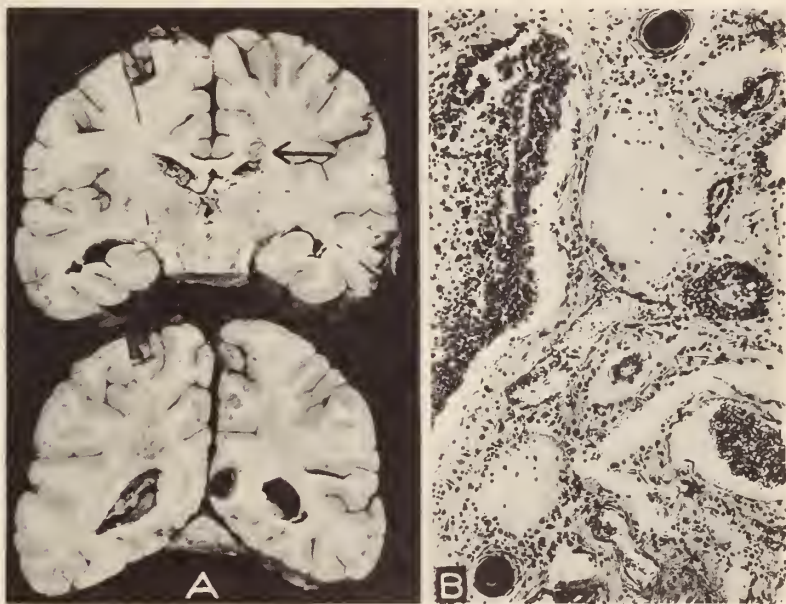
Fig. 4 (Case 4).   A. Photograph of coronal sections of brain illustrating metastatic abscesses. B. Section of the chorioid plexus showing miliary abscesses and psammoma bodies (Hematoxylin and eosin stain).

incised, was seen to cover a softened, brownish red mass, sharply demarcated and about one centimeter in diameter.   From it oozed brown purulent material. A similar area, yellowish in color, was visible on the medial surface of the parietal lobe at the junction of the gyrus cinguli with the precuneus.   On further sectioning, several other small, well delimited abscesses were found, one in the corpus callosum, another in the cortex of the mesial surface of the right occipital lobe (Fig. 4 A), and a third in the left occipital lobe just above the posterior horn.   The chorioid plexus of the left lateral ventricle was thickened and covered with exudate (Fig. 4 A). The *general post mortem examination* revealed a small empyemic pocket in the left chest, its pus revealing, on smear, gram positive cocci in chains.

Microscopic Anatomy.   Sections through one of the small abscesses revealed a core of necrotic and degenerated neutrophilic leucocytes.   Within the core were

also to be seen five or six irregularly shaped basophilic bodies about the periphery of which radiated pinkish fibers. Under longer magnification these proved to be composed of chains of cocci aggregated into dense masses. About the wall of the abscess was an area of well marked gliosis containing numerous small hemorrhages and foci of leucocytic infiltration. Peripheral to this was an area of brain tissue which showed profound degenerative changes. The meninges were infiltrated with lymphocytes and macrophages. Sections taken of the chorioid plexus (Fig. 4 B) and the ependyma showed them to be the seats of marked suppuration in the form of minute abscesses.

Comment by Dr. Globus. The diagnosis of a metastatic brain abscess and secondary suppurative meningitis was made during the clinical course, in spite of the fact that the known pulmonary condition was considered completely healed. The multiplicity of the brain lesions points to their secondary character.

Case 5. *Metastatic Brain Abscess. Dr. Grant Levin*

History (Adm. 378810). An Italian male, aged 64 years, entered the hospital on April 15, 1935, complaining of acute impairment of vision of eight days' duration. Two previous admissions to the hospital had been concerned with the treatment of a pulmonary abscess, the symptoms of which had begun in October, 1933. An earlier incident referable to his eyesight had occurred twenty-five years previously. He had at that time suffered a temporarily blinding inflammation of the left eye. Treated by "drops," his vision was thereafter completely restored. Another disturbance of vision had occurred in 1932 when he began to notice slight clouding of vision affecting both eyes. This impairment continued without change for three years until eight days before admission when, abruptly, the sight in the left eye became so poor that he was unable to avoid obstacles in his path. Three days later it was noted that he held his left arm unnaturally at his side and was unable to manage his left leg in walking. In the two days preceding admission he complained of severe generalized headache.

Examination. There were several thoracotomy scars on the right side, where the breath sounds and vocal fremitus were increased. The area of cardiac dulness was slightly enlarged to the left and the blood pressure was 170 systolic and 90 diastolic. Tenderness was present diffusely over the entire dome of the skull. The gait was tottering and uncertain with constant falling to the left. The patient was able to count fingers with the right eye at a distance of ten feet, but could distinguish only light with the left. The left pupil was larger than the right and was fixed to light. The right visual field was defective in the inferior nasal quadrant and both optic discs displayed a metallic pallor, that of the left being more marked. The left arm was held in flexion at the wrist and elbow, partook to a greater extent in a generalized spasticity and ataxia of the extremities, and was tremulous. There was a generalized hyperreflexia, but the right patellar and left Achilles jerks were more active. The abdominal reflexes were absent and there were bilateral equivocal Babinski and Oppenheim signs.

Laboratory Data. The cerebrospinal fluid was under an initial pressure of 140 mm. of water and contained 60 lymphocytes per cu. mm. There were a few pus cells in the urine.

Course. Five days after admission it was found that the appearance of the patient's eyes and his ocular difficulties were due to bilateral glaucoma. The

remainder of his signs and symptoms were considered to be due to a lesion in the right temporal lobe, either neoplastic or inflammatory in character, with the probability favoring an abscess secondary to the pulmonary infection.

Two days later a subtemporal decompression was made on the right side as the first of two contemplated operative stages. Two hours after operation the patient sank into deep stupor and his cerebrospinal fluid pressure was determined to be 260 mm. of water. It was deemed imperative to return him to surgery where the decompression was enlarged and a few clots were removed. Exploration with a brain needle revealed no abscess. Following this his failure was progressive and exitus occurred two days later.

Necropsy Findings. Gross Anatomy. A soft, dark red area of disorganized tissue was seen to occupy a field 3 by 3 cm. at the site of the operation in the right
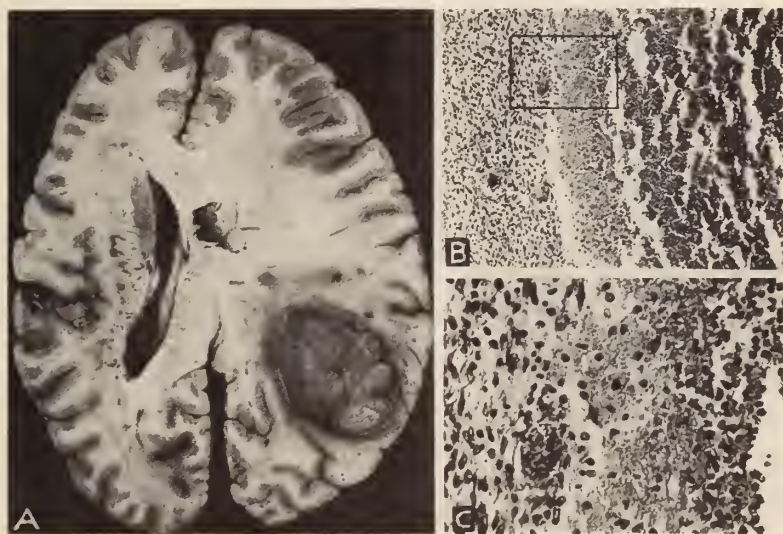
FIG. 5 (Case 5). A. Photograph of horizontal section of brain illustrating abscess in right parieto-occipital lobe. B. Section of abscess showing necrotic center and wall (Hematoxylin and eosin stain). C. Higher magnification of rectangular area in B.

middle and superior temporal gyri. The surrounding convolutions were soft and compressed. In the right parietal lobe, involving the angular and supramarginal gyri was a large, round, fluctuant bulge, yellowish green in color and overlaid by arachnoid in which the vessels were engorged. Here too, the neighboring brain tissue was softer than normal. When incised, this bulge yielded thick, greenish pus with a foul odor. There was no bacterial growth on culture.

On sectioning, the abscess cavity was found to occupy the posterior half of the parietal and an anterior portion of the occipital lobe on the right side (Fig. 5 A). It measured 3 cm. in diameter, was lined by a fairly well defined capsule, and was surrounded by a definite zone of congestion. In the upper lobe of the right lung there was a bilocular cavity representing a healed abscess. Bronchiectasis of the cylindrical type was also present.

Microscopic Anatomy. The meninges and arterial walls were moderately thickened. There was a clear cross section of the wall of an abscess cavity lying within the cerebral cortex. Centrally there was an agglomeration of leucocytic debris sourrounded by a thick layer of leucocytes and plasma cells. Peripheral to this was a layer of loose connective tissue in which were numerous fibroblasts and young blood vessels (Fig. 5 B & C). Still more peripherally, without the limits of the abscess proper, there was an increase in the glia and dense lymphocytic perivascular cuffing. No bacteria were seen.

Comment by Dr. Globus. It is obvious that the impairment and final loss of vision are unrelated to the cerebral lesion. Of special note is the formation of a metastatic focus in the brain at a time when the pulmonary lesion seemed to be quiescent or healed.

Case 6.   *Spongioneuroblastoma of the Brain Stem.   Dr. Theodore Meltzer*

History (Adm. 386526).   A three and one-half year old female child was admitted to the hospital on November 8, 1935. Eight weeks before admission the child, while asleep, fell out of the carriage and struck the left side of her head against the sidewalk. She became unconscious and suffered a generalized convulsive seizure which was reported to have lasted twenty minutes. During the following week she was irritable and cried a good deal. One week after the accident there developed a right facial paralysis, a drooping of the left eyelid and an inability to turn the right eye outward. Three weeks after the accident it was noted that the child stumbled and would sometimes fall. She was not inclined to use her left arm. About this time she vomited once. For the next five weeks until she was admitted to the hospital she had been alternately stuporous, apathetic, irritable and depressed. There was loss of weight with marked polydipsia and polyphagia.

Examination. The child was dull, lethargic, and incontinent of urine. The right palpebral fissure was larger than the left, probably due to ptosis of the left upper eyelid. The right pupil was larger. Both pupils reacted to light and in accommodation. Except for slight vertical movement, the right eyeball was fixed. Both abducens nerves were paralyzed. There was a right peripheral facial paralysis. The deep reflexes in the upper and lower extremities on the left side were exaggerated and a Babinski sign was present on that side. The muscles of the left lower extremity were spastic.

Course. It was at first felt that the patient had multiple hemorrhagic lesions in the brain stem, but later an expanding lesion, probably in the nature of a tuberculoma was considered. The child's condition remained, however, too grave to undertake aerographic studies. Her condition remained the same until ten days after admission (November 18, 1935) when she vomited and developed a temperature of 103°F. A severe upper respiratory infection developed from which she recovered, but otherwise remained in a state of dullness and torpidity. This continued until December 17 when she began to vomit. A lumbar puncture was done and it yielded cerebrospinal fluid under an initial pressure of 160 mm. of water. The fundi, which were previously normal, now showed slight blurring of the right disc. She gradually declined and died on December 29, 1935, seven weeks after admission.

Necropsy Findings. Gross Anatomy. The convolutions of the brain were markedly flattened. The entire brain stem, especially the pons and midbrain, was enlarged and cystic to palpation. Upon sectioning a large soft mass was exposed.

This was found to replace nearly all of the brain stem and extend upward into the caudal end of the midbrain surrounding the fourth ventricle. The mass was in part hemorrhagic in appearance, in others, it was filled with a greenish-brown viscid material (Fig. 6 A).

Microscopic Anatomy. Sections of the tumor displayed a very cellular structure. The cells tended to be spindle-shaped with darkly stained vesicular, elongated nuclei. In some parts of the tumor the cells were arranged around blood vessels. In other parts they formed strands which interlaced with one another. Special staining methods displayed many bipolar spongioblasts and other cells of less
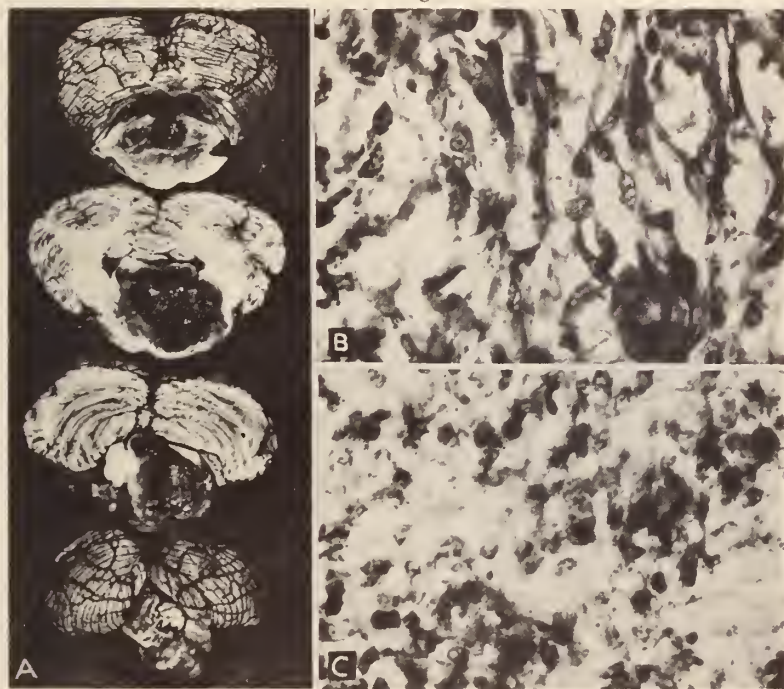
Fig. 6 (Case 6). A. Photograph of brain stem illustrating situation of **tumor.** B. Section of tumor showing many spongioblasts (Bielschowsky stain). C. Section of tumor showing numerous undifferentiated ganglion cells (Nissl stain).

differentiated character (Fig. 6 B). In sections of the midbrain many ganglion cells of undifferentiated character were seen (Fig. 6 C).

Comment by Dr. Globus. Of particular interest here is the history of trauma which, it is alleged, precipitated the illness of the child. The character of the tumor, its extent and site all speak against a possible relationship between the fall of the child and the development of the tumor.

Case 7. Glioneuroma of the Right Cerebral Hemisphere. Dr. Theodore Meltzer

History (Adm. 396992). A 50 year old male was admitted to the hospital on August 11, 1936. On one occasion, four years before admission, the patient suddenly collapsed and lost consciousness for a period of ten to fifteen minutes. There

were no convulsions and he felt perfectly well afterwards. Four similar episodes took place during the following year. Three years before admission the patient commenced to experience chills followed by sensation of heat and sweating. They were confined to the upper and lower extremities and occurred nearly every day. One year before admission each episode was preceded by the patient experiencing the smell of rotten eggs. Seven months before admission he felt, for the first time, pain in the head. This began in the occipital region and radiated forward over the crown and temples. The pain subsided for a few months and then recommenced, but with added features, such as blurring of vision and noises in the head. One month before admission he found that the left thumb was less useful than usual when performing fine movements. Mentally, he had been suffering from lack of interest and initiative. He was depressed, dissatisfied, and disturbed by the hallucinations of smell (also sight?).

Examination. The patient was confused, disoriented and showed some difficulty in comprehending directions. The blood pressure was 140 mm. of mercury systolic and 100 mm. of mercury diastolic. He could detect the smell of coffee in the right nostril. The left pupil was larger than the right; both reacted well to light and in accommodation. Bilateral papilledema was present, more advanced on the right. There was a slight left central facial paralysis. All abdominal reflexes were absent except for the left upper reflex which reacted slightly. The left biceps jerk was more active than the right but the right knee jerk was more active than the left. There was some diminution of vibration sense in the left foot. There was some clumsiness when performing skilled movements with the left hand, and some tremor of the outstretched fingers, this being more marked on the left side. A lumbar puncture yielded clear cerebrospinal fluid under an initial pressure of 140 mm. of water. Apart from a slight increase of total protein content, the fluid was normal. X-ray examination of the skull revealed irregular areas of calcification in the right temporal region.

Course. Apart from headaches, the patient's condition remained unchanged until six days after admission when he suddenly went into deep coma, and displayed the picture of decerebrate rigidity. An emergency ventriculography was then performed. This showed displacement of the ventricular system to the left, compression of the right lateral ventricle and dilatation of the left lateral ventricle. An expanding lesion in the temporal lobe on the right side was diagnosed. Craniotomy was performed and a large tumor was disclosed in the right temporal region. Only part of it was removed in order to allow for decompression, but the patient declined rapidly and died the same day.

Necropsy Findings. Gross Anatomy. The right cerebral hemisphere was larger than the left, and contained a tumor in the right frontotemporal region. It measured approximately 4 cm. by 3 cm. and extended for about 2 cm. into the substance of the brain. The tumor was hemorrhagic and necrotic. When sectioned, the brain displayed an enlarged and deformed ventricular system and an extensive hemorrhagic area in the basis pedunculi, extending into the tegmentum of the pons.

Microscopic Anatomy. The tumor was densely cellular. The cells contained nuclei which were vesicular and round or oval in shape. Special silver staining methods revealed their gliogenous character. Throughout the tumor there were many large hemorrhages and numerous extravasations of blood elements (Fig.

7 A). Sections stained with the Nissl method showed the presence of many ganglion cells which were in a state of partial development (Fig. 7 B). One section displayed many irregular areas of calcification (Fig. 7 A).

Comment by Dr. Globus. This tumor form was considered until recently as very rare. Cushing in his review of two thousand verified brain tumors found only three such instances, two of which were located in the pineal body and one of which was doubtful as to histologic character. In the Mount Sinai collection of supratentorial tumors of neuroectodermal derivation, consisting of one hundred and seventy cases, twelve such tumors were found. Their recognition was made possible by the use of the Nissl stain, an older staining method. These tumors show certain clinical features in common. There is a precipitate onset ushered in either by a convulsive seizure of the Jacksonian variety or by a petit mal
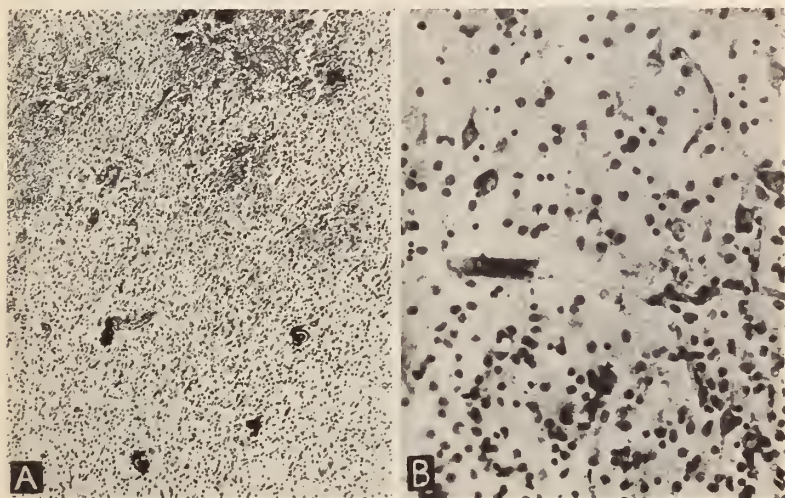
Fig. 7 (Case 7). A. Section showing areas of hemorrhage and calcification (Hematoxylin and eosin stain). B. Sections showing numerous ganglion cells (Hematoxylin and eosin stain).

attack in the nature of a brief period of unconsciousness, or a short episode of aphasia. This, with but a few exceptions, is followed by an increasing frequency of such attacks, which may vary from time to time in their character and intensity. Gradual, intellectual disintegration and the development of more discrete localizing signs follow.

Case 8. Miliary Metastatic Carcinoma of the Brain and Meninges.
Dr. Lawrence Weinberger

History (Adm. 388099). A woman, aged 52, four months before admission to the hospital began to experience excessive drowsiness which was shortly followed by intermittent headaches, dizziness and vomiting after meals. A dropped womb was diagnosed and a hysterectomy was performed elsewhere. Following this operation, the vomiting increased in severity up to the point where she required therapy to overcome dehydration. Her headaches became agonizing. She

became disoriented, developed marked speech defects, and began to lose her vision. Coincidental with these symptoms there had been marked loss of weight. Her gait became staggering and this was attributed to weakness. Further investigation disclosed that the patient had a tumor excised from her mouth four years prior to the onset of her illness. The nature of the tumor could not be ascertained.

Examination. The patient was admitted to the hospital in extremis. She was cyanotic and dyspneic, her pulse was thready and rapid and the lung fields were filled with râles. She was considerably emaciated. The liver was palpable. There were no enlargements of any of the regional lymph nodes. The pupils

FIG. 8 (Case 8). Photograph of horizontal section of the brain illustrating numerous metastatic nodules.

were unequal but reacted to light and the fundi were normal. There was flattening of the left side of the face. The pharyngeal reflexes were absent. There was slight nuchal rigidity, the reflexes on the left side of the body were more active than the right, but there were no pathological reflexes. The abdominal reflexes could not be elicited.

Course. The consensus of opinion was that the patient had an unlocalizable brain tumor. The patient expired shortly after admission. A lumbar puncture performed after death revealed clear fluid.

Necropsy Findings. Gross Anatomy. The autopsy was limited to the head. The brain was swollen and the gyri flattened, particularly in the posterior half of

the right hemisphere. There was a thin film of subdural blood on the convexity of the hemispheres. When the brain was sectioned after fixation, it appeared normal at first glance, but with closer inspection it was noted that all parts of the brain were studded with pin-head to millet-seed sized grayish, opalescent nodules (Fig. 8).

Microscopic Anatomy. Examination of the nodules showed these to be neoplastic. The cells were large and polyhedral with abundant granular cytoplasm
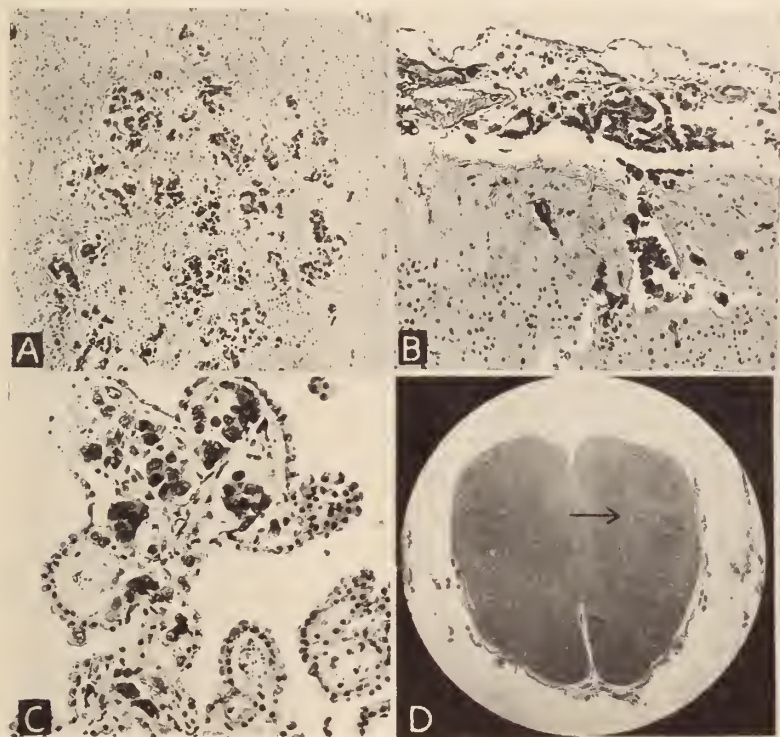
Fig. 9 (Case 8). A. Section showing arrangement of cells in neoplastic nodule (Hematoxylin and eosin stain). B. Section showing neoplastic cells in leptomeninges with extension along the pial vessels (Hematoxylin and eosin stain). C. Section of the chorioid plexus showing tumor cells in capillaries (Hematoxylin and eosin stain). D. Section of the lower part of the medulla oblongata showing neoplastic nodule (Hematoxylin and eosin stain).

and contained deeply stained oval nuclei possessing nucleoli (Fig. 9 A). The meninges were everywhere thickly infiltrated with neoplastic cells which, in some situations, arranged themselves in rows against a strand of connective tissue simulating a basement membrane (Fig. 9 B). Section through the chorioid plexus showed neoplastic cells occupying the lumina of the chorioidal capillaries (Fig. 9 C). The neoplastic cells were grouped in rows encircling the small terminal capillaries. They usually were arranged about capillaries branching off a single

vessel and in this situation a cross section appeared like a bouquet.   Tumor cells were occasionally seen within the parenchymal vessels.   Sections through the lower part of the medulla oblongata showed metastatic nodules within its substance (Fig. 9 D).

Comment by Dr. Globus.   The distribution of the tumor cells about blood vessels filling the perivascular space and the presence of tumor cells in both the subarachnoid space and the chorioid plexus, indicate that the tumor cells reached the brain by way of the blood stream.   These were discharged by the chorioid plexus into the cerebrospinal fluid which carried them to the subarachnoid space and into the brain by way of the perivascular spaces.

ABSTRACTS

Members of the hospital staff and the out-patient department of The
Mount Sinai Hospital are invited to submit for publication in this column
brief abstracts of their articles appearing in other journals.

The Reduction of Some Adsorbed Oxidation-Reduction Indicators. H. A. ABRAMSON
AND I. R. TAYLOR. J. Phys. Chem. 40: 579, April 1936.

Oxidation processes in biological systems may take place at or in the presence of
surfaces. By a study of the reversibility of adsorbed oxidation-reduction indicators
like methylene blue, litmus and phenosafranine adsorbed on filter paper, cotton,
keratin etc., it is shown that the electrometric measurement of the potential need
not indicate the potential at the surface even though "equilibrium" has been at-
tained electrometrically. Under proper conditions all of the dyes investigated retain
their ability to be oxidized and reduced reversibly even though adsorbed. This
indicates that the physico-chemical processes involved in the adsorption reaction
do not interfere with the oxidation-reduction mechanisms to an appreciable extent.

Temperature of the Skin Surface. W. BIERMAN. J. A. M. A. 106: 1158, April 1936.

Normal variations in the temperature of the skin surface are pointed out. The
influence of age, metabolic changes, cold, and fever are described. Skin surface
temperature may be used as a diagnostic procedure in peripheral vascular diseases
and in other medical and neurologic conditions.

The effects of tobacco, coffee, and alcohol upon the peripheral circulation are
indicated. The therapeutic value of drugs and of physical measures may be deter-
mined by changes in skin surface temperature.

*Reactivity of Malignant Neoplasms to Bacterial Filtrates II. Relation of Mortality to
Hemorrhagic Necrosis and Regression Elicited by Certain Bacterial Filtrates.*
G. SHWARTZMAN. Arch. Path. 21: 509, April 1936.

Bacterial substances capable of eliciting the phenomenon of local skin reactivity
to bacterial filtrates in rabbits produce, upon intravenous injection, hemorrhagic
necrosis and regression of transplantable malignant tumors of guinea pigs, mice and
rats. There is, however, a high death rate in animals thus treated. In experiments
on the phenomenon of local skin reactivity to bacterial filtrates in rabbits it was
observed that, in certain proportions, mixtures of *B. typhosus* "agar washings"
filtrates with homologous antisera possess a high phenomenon-producing and low
lethal potency. Studies were then made on the effect of single intravenous injections
of these mixtures and of toxic filtrates alone upon mice bearing twelve days old
sarcoma 180. In certain proportions, mixtures of *B. typhosus* filtrates with homol-
ogous antisera possess a comparatively low lethal potency and yet elicit prompt and
intense hemorrhagic necrosis with subsequent complete regression of sarcoma 180
in a high percentage of mice, well above normal expectancy.

Electrocardiogram in Fever; Changes in Induced Hyperpyrexia. H. VESELL AND W. BIERMAN. Am. J. Med. Sci. 191: 484, April 1936.

Observations were made of electrocardiographic changes caused by physically induced fever of three to five hours' duration. Changes in the heart rate are described.

The alternations of electrocardiogram waves were not uniform. The P and T waves were increased in size almost as frequently as they were decreased. The R wave, however, most often became smaller and the P-R and Q-R-S intervals in most instances were shortened. The RT level was usually depressed, never elevated.

Of special significance was a transformation of several normal amplitudes or intervals to abnormal ones, as well as the reverse. This involved particularly the R and T amplitudes. The development of a prominent Q_3 in one instance is worth mentioning.

The mechanism of electrocardiographic changes is probably through reflexes, tachycardia, local cardiac, and general chemical and physiologic alterations. None of the electrocardiographic changes were permanent. No inference can be drawn that the fever produced any harmful effects upon the heart.

Integration of the Child—The Goal of the Educational Program. I. S. WILE. Ment. Hyg. 20: 249, April 1936.

Children possess innate possibilities for responsibility and adaptation. Health, intellectual interest, vocational application, and social cooperation are not only expressions of individuality, but also highly desirable as educational aims. The capacity to adjust, to remain "whole," and to live "whole" can be facilitated through an educational program that sees the child as a "whole." The integration of the child constitutes a positive aim of education. It is a function of an educational program that makes right adjustments in personality possible as a preliminary to right thinking, feeling, relationships, and living.

Primary Pneumococcus Type XXII Meningitis. S. HIRSCH. J. A. M. A. 106: 1562, May 1936.

A case of pneumococcus type XXII meningitis is rarely reported. In this instance a man, aged 53, awakened one morning with slight but rapidly intensifying frontal headache. Within twenty-four hours he developed somnolence and urinary retention. There was a rapid onset of signs of meningeal irritation. Lumbar puncture yielded purulent fluid under increased pressure. This fluid was negative for organisms on smear and culture. The following day a cisternal puncture was done yielding purulent fluid which was also negative on smear but yielded a pneumococcus type XXII on culture. Death ensued on the fourth day after the onset of the illness.

Postpneumonic Residual Infiltration; Observation on 10 Patients Followed From 2 to 10 Years After Original Admission. J. L. KOHN. Am. J. Dis. Child. 51:1101, May 1936.

The report is concerned with a group of ten children, who continued to have symptoms of pulmonary infiltration, from two to ten years, after their original acute nontuberculous pulmonary involvement. They were seen at frequent intervals after the onset of pneumonia. The effect of intercurrent illness was noted. Their clinical courses were analyzed in respect to persistence of roentgen findings, physical signs and symptoms. Allergic sensitization or the involvement of the accessory nasal sinuses did not seem to be important in aggravating or maintaining pulmonary infiltration. Only one child died. The remainder are developing normally, without any signs of suppurative pulmonary infiltration, although most of these patients still have symptoms.

Pneumonia in Children: Survey of 1000 Cases with Attempted Follow-Up. J. L. KOHN AND S. B. WEINER. Am. J. Dis. Child. 51: 1095, May 1936.

A survey of one thousand cases of primary non-tuberculosis pneumonia was made. In only seven was there a recent history of measles or pertussis. An attempt was made to follow the patients after discharge, in order to trace the evolution of subacute and chronic pulmonary disease. Eighty per cent left the hospital alive. On discharge, forty per cent of these patients had positive pulmonary physical findings and about fifty-seven per cent had evidence of infiltration on roentgenological examination. In a high percentage of the cases, all evidence of disease had disappeared in less than six months. The severity of the initial illness was no criterion of the persistence of pulmonary disease.

This study suggests that severe bronchiectasis rarely follows the ordinary acute pulmonary infections.

Atypical Roentgen Appearance of Pulmonary Infarction in Patients with Heart Failure. H. LEVY. Am. J. Roentgenol. 35: 635, May 1936.

In a patient with heart disease an intercurrent pulmonary lesion should arouse the suspicion that it may be the result of infarction. The shadows cast by such lesions are occasionally atypical and simulate neoplastic, inflammatory, and, less commonly, cystic lesions. They often lead to erroneous diagnoses. Although peripherally situated, an infarct, if located posteriorly or anteriorly, casts a diagnostically confusing para-hilar or central shadow. Lateral films, therefore, are also necessary. Two cases with roentgenographically atypical infarcts are described. Both occurred in elderly patients with pulmonary congestion and heart failure secondary to coronary artery disease. The importance of pulmonary congestion as a factor in the atypical situation and roentgen appearance of pulmonary infarcts is stressed. The persistence of residua of infarct shadows over months and years is noted.

Electrokinetic Phenomena XII. Electroosmotic and Electrophoretic Mobilities of Protein Surfaces in Dilute Salt Solution. L. S. MOYER AND H. A. ABRAMSON. J. Gen. Physiol., 19: 5, 727, May 1936.

It is shown experimentally that the ratio of electroosmotic to electrophoretic mobility of certain protein surfaces is very close to 1.0, even in very dilute solutions of electrolytes. This series of observations lends simplicity to the theoretical and experimental approach to the study of the effects of salts on protein surfaces.

Value of Prognostic Venom Reaction in Thrombocytopenic Purpura. S. M. PECK, N. ROSENTHAL, AND L. A. ERF. J. A. M. A. 106: 1783, May 1936.

An intradermal moccasin snake venom test has been used as a prognostic measure in essential thrombocytopenic purpura hemorrhagica. Persistence of a positive reaction in successive tests, or a reversal to a negative reaction, is of value in determining the trend of the purpuric state.

Subcutaneous injections of moccasin snake venom have been employed as a therapeutic measure in chronic purpura hemorrhagica. The procedure has apparently been of value in twenty-two of the thirty-four cases in which it was used.

The effect of subcutaneous venom injections and the trend of the intracutaneous venom test are important in considering the indication for and prognosis of splenectomy.

Recurrence of Paroxysmal Auricular Fibrillation After Permanent Relief of Hyperthyroidism by Subtotal Thyroidectomy. E. P. BOAS. J. A. M. A. 106: 2238, June 1936.

In a woman, aged 50 years, following successful operation for hyperthyroidism with established auricular fibrillation, normal sinus rhythm was restored post-operatively with the use of quinidine. Nineteen months later, immediately after two operations of a three stage resection for colonic neoplasm, transient auricular fibrillation occurred, subsiding spontaneously after twelve hours on each occasion. In the absence of recurrent hyperthyroidism and of significant cardiovascular disease, it is suggested that an altered metabolic state of the heart muscle, persisting after the hyperthyroidism has been cured, may favor the recurrence of auricular fibrillation.

Abdominal Puncture in Diagnosis of Peritonitis in Childhood. B. S. DENZER. J. Ped. 8: 741, June 1936.

The method of abdominal puncture of Neuhof and Cohn has been used in prefer-ence to that described by the author fifteen years ago. Abdominal puncture is indi-cated wherever there is doubt as to the presence and nature of a peritoneal exudate. It is of particular service in diagnosis in infants and children because at this age abdominal signs are even more confusing than in adults and subjective data are unavailable. The differential diagnosis between streptococcus and pneumococcus peritonitis on the one hand, and appendicitis on the other, is radically different in these two groups of cases. In the former (streptococcus and pneumococcus peritoni-tis), transfusion and continuous intravenous therapy may avoid operation altogether and, even when operation is necessary, a different type of procedure is indicated and it is done usually later in the illness. It is most important to emphasize the safety of the procedure and the simplicity of the technique.

The Shwartzman Phenomenon in the Kidneys of Rabbits. Observations on effects of intravenous administration of bacterial filtrates. I. E. GERBER. Arch. Path. 21: 776, June 1936.

The Shwartzman phenomenon was produced in the kidneys of rabbits by the injection of filtrates of B. typhosus and meningococcus into the general circulation in two doses, twenty-four hours apart. Animals which received only one intrave-nous dose did not show renal changes, which consisted of thrombosis of the glomerular capillaries, focal tubular necrosis, and focal or diffuse cortical necrosis with necro-tizing arteritis of the interlobular vessels. Venous and capillary thrombi, and degenerative changes in the heart, lungs, liver, spleen, bone marrow and adrenals were found in both groups of animals. The renal lesions, as well as the thrombotic and degenerative changes in the other organs, were morphologically similar to those sometimes observed in infectious conditions in humans, and in spontaneous and experimental hog cholera. It is suggested that the lesions in humans, as well as in hog cholera, are due to the effects of circulating bacterial toxins and are patho-genetically comparable to the experimental lesions produced by the author.

Electrocardiographic Changes Following Coronary Sinus Occlusion in the Dog's Heart. LOUIS GROSS, M.D., GERTRUDE SILVERMAN, M.D., AND ARTHUR M. MASTER, M.D. Am. Heart J. 2: 734, June 1936.

Partial and complete obturation of the mouth of the coronary sinus was produced in forty-one dogs by means of a variety of procedures. Among these were ligation, and the injection of escharotics into the lumen of, or around, the coronary sinus. These procedures were employed alone or in combinations. In fifteen additional dogs they were employed without producing appreciable coronary sinus obturation, as determined at autopsy.

Following complete obturation, there occurred dilatation of the heart, engorge-ment of the superficial veins, and cyanosis of the left ventricle up to, and slightly beyond, the interventricular grooves. Occasionally small ecchymoses were also observed. The electrocardiographic findings, resulting from complete or partial

occlusion, were notching and downward direction of the main QRS deflection, eleva-
tion of the R-T transition, occasional inversion of the T-waves, and temporary
slowing of the heart rate. These findings were most constant when occlusion was
complete and sudden. The almost invariable occurrence of inversion of the T-wave
when complete obturation was preceded by dissection of the coronary sinus raises a
question as to the possible rôle played by this additional injury in the production of
the electrocardiographic changes. Since the RST changes occurred even in the
absence of local injury, it appears that they were probably associated with conges-
tion of the heart. A contributing factor in causing inversion of the QRS deflection
may have been the change in position or rotation of the heart produced by the con-
gestion which occurred mainly in the left chambers.

No changes were found following the placing of the ligature around the coronary
sinus without occlusion. Partial obturation produced electrocardiographic findings
similar to complete occlusion, but the changes were less constant in their occurrence.
All electrocardiographic changes tended to disappear within a period of from two to
four weeks after the occlusion was produced.

The RST changes, when present, were similar to those observed following acute
coronary occlusion, but unlike the latter, they did not present the pathognomonic
steady progression into inverted T-waves. Thus, following coronary sinus occlusion,
the heart gradually readjusts itself, and the electrocardiographic tracings return to
normal.

It is suggested that the electrocardiographic findings reported may result from a
temporary injury of the myocardium due to oxygen insufficiency attendant on venous
congestion. Other factors, such as local injury due to manipulation and change in
the position of the heart, probably play minor rôles.

Thrombosis of the Lateral Sinus and Jugular Bulb of Non-otitic Origin. S. KARELITZ.
 Am. J. Dis. Child. 51: 1349, June 1936.

Three cases of retrograde jugular bulb and lateral sinus thrombosis, with a new
otitic manifestation or clinical sign are described. Hitherto this condition has been
recognized on post mortem examination only. The painless engorgement of tym-
panic membrane, in the absence of hearing disturbance or any signs of mastoiditis, is
suggestive of occluding thrombus in the bulb and lateral sinus. When chills and
other evidence of sepsis are present, the above sign should be used as an indication for
surgical exploration of the lateral sinus and internal jugular vein. This condition
should be suspected in cases of pharyngeal and neck infections and when bacteremia
is present.

Disseminated Spinal Arachnoiditis. Its Diagnosis and Treatment with Roentgen Rays.
 H. SELINSKY. Arch. Neurol. & Psychiat. 35: 1262, June 1936.

Eight cases are presented in which a syndrome characterized by "burning" pain
in one or more extremities for several months was noted. The objective signs pointed
to a polyradicular process, infrequently associated with signs of disease of the spinal
cord. The Queckenstedt test and iodolography are indispensable aids in leading to a
correct diagnosis in cases of disseminated spinal arachnoiditis. The etiology of this
condition is unknown, but there is some evidence to suggest an extension of a focal
infection. High voltage roentgen therapy exerts a definitely ameliorating effect
which is variable in duration. Recurrence of pain is usually relieved by a repetition
of the roentgen treatment.

Essential Xanthomatosis. Treatment with Cholesterol-Free Diet in Two Cases. W.
 M. SPERRY AND B. SCHICK. Am. J. Dis. Child. 51: 1372, June 1936.

A case of essential xanthomatosis occurring in a child is described. The case is of
interest because of certain features, particularly the presence of xanthelasma pal-

pebrarum and a marked arcus corneae, which are more characteristic of the advanced form of the disease as it occurs in adults. A description of such an advanced case in an adult is included for comparison.

Treatment for considerable periods of time with a cholesterol-free diet had no definite effect, either on the hypercholesteremia or on the clinical picture of either of the patients. The results are in contrast to those obtained by other investigators, who have reported a marked decrease in the cholesterol content of the blood serum and an improvement in the clinical condition following the administration of similar cholesterol-free diets to patients with essential xanthomatosis. There appear to be marked differences in the pathogenesis of this disease, since some patients react favorably to a cholesterol-free diet while others are not affected by the same treatment. All patients with essential xanthomatosis should be treated with a cholesterol-free diet for a considerable period of time, since a certain number may be expected to react favorably.

In the cases reported the proportion of combined cholesterol to free cholesterol in the serum was normal; in the previously described cases, in which the patients showed improvement on a cholesterol-free diet, the ratio of combined cholesterol to free cholesterol was highly abnormal. This may prove to be a point of diagnostic importance, and we suggest that the amounts of combined cholesterol and free cholesterol be determined before and during treatment with a cholesterol-free diet in all cases of essential xanthomatosis.

Observations on Ulcerations Adjacent to Experimental Gastric Pouches in Dogs. A. WINKELSTEIN. Am. J. Digest. Dis. & Nutrition. 3: 229, June 1936.

While studying the chemical phase of gastric secretion in dogs by means of a subcutaneous, nerveless Klein pouch, large ulcerations were noted in the adjacent abdominal wall. During estrus, these ulcerations healed and the pouch secretion diminished. During lactation, the ulcerations enlarged and the secretion increased. With the administration of Theelin, such ulcerations decreased in size, while after Antuitrin "S" they increased. These experiments are reported to stimulate further investigations on the possible relationship of the ductless glands to gastric secretion, healing processes, and internal peptic ulcer in man.

Lipoma of the Extremities. E. M. BICK. Ann. Surg. 104: 139, July 1936.

These tumors represent more than 50 per cent of soft tissue tumors of the extremities. They occur predominantly about the shoulder and gluteal or subgluteal regions. They may appear in subcutaneous fat, in muscle tissue, or in bones or joint tissues. Liposarcoma is unusual, but not a rarity. In 20 per cent, lipoma are multiple. They may or may not be encapsulated. They should be excised whenever they are subject to minor traumata or pressures.

Labyrinthitis Secondary to Meningococcic Meningitis. J. G. DRUSS. Arch. Otolaryng. 24: 1, 19, July 1936.

Deafness is not an uncommon sequel of meningococcic meningitis. The deafness is usually bilateral and often complete. It is usually due to a labyrinthitis secondary to an extension of the infection from the meninges. Extension takes place along the nerves in the internal auditory meatus, through the aqueductus cochleae and by way of the blood stream. This report is based on a study of serial sections of five temporal bones which showed evidence of the early and late pathologic changes in the labyrinth secondary to meningococcic meningitis. The early pathologic changes consisted mainly of hemorrhagic and serofibrinous exudate in the various parts of the labyrinth and atrophy and degeneration of the sensory nerve endings. The late pathologic changes are those usually seen with healed labyrinthitis. Almost the entire labyrinth is replaced by new bone—evidence of a reparative process.

On the basis of clinical and pathologic evidence that early invasion of the laby-
rinth is very common, invasion taking place by way of the cerebrospinal fluid and
through the blood stream, treatment administered through both these channels at a
very early date is suggested.

Complications of Acute Sinusitis with Special Reference to Bacteremias.   J. I. GOLD-
     MAN.   Laryngoscope 46: 500, July 1936.
   This report is especially concerned with the relationship between bacteremias and
acute paranasal sinus infections and their complications.   An analysis was also made
of the important features of these complications.
   Three hundred cases of acute sinusitis admitted to The Mount Sinai Hospital were
studied.   These cases were analyzed according to the following groups: uncompli-
cated cases with temperature below 103°F.; uncomplicated cases with temperature
above 103°F.; and cases with complications.   In the first two groups bacterial growth
was not obtained in any blood culture although the blood was cultured in 37 per cent
of the uncomplicated cases with a temperature above 103°F.
   There were ninety cases of acute sinusitis that presented in each instance some
complication originating from that infection.   These complications were grouped
as follows: (1) orbital cellulitis, (2) oribital abscess, (3) osteomyelitis of the skull,
(4) acute purulent meningitis, (5) brain abscess, (6) cavernous sinus thrombosis
and (7) miscellaneous infections.   Of these ninety patients, thirty-five died—a mor-
tality rate of 35 per cent.   This high death rate was essentially due to the serious
complications of acute purulent meningitis, cavernous sinus thrombosis, brain ab-
scess and osteomyelitis of the skull.   Blood culture studies were made on thirty-five
of the ninety patients, and bacterial growth was obtained from the blood of sixteen,
or 44 per cent of the cases.
   The findings in this study appeared to indicate that, except for possibly an occa-
sional case, the occurrence of a positive blood culture in acute sinusitis points to the
coexistence of a complication or some associated systemic infection.   The study
further suggested that routine blood culture in acute sinus infections might prove to
be of value in helping to determine the presence of a complication.

Moccasin Snake (Ancistrodon Piscivorus) Venom Therapy for Recurrent Epistaxis.
     J. L. GOLDMAN.   Arch. Otolaryng.   24: 59, July 1936.
   This clinical study illustrates the beneficial effect of moccasin snake venom in
the treatment of recurrent epistaxis.   The results of forty-two patients who had
received only this form of therapy were reported.   The following classification was
formulated according to the source of bleeding: (1) telangiectasia of the nasal sep-
tum, (2) ulcerations of the nasal septum, (3) bleeding without visible source and (4)
hemangioma of the nasal septum.   The cases in each of the groups were analyzed.
The venom therapy was effective in practically all instances, either in completely
arresting and controlling the nasal bleeding or in markedly diminishing its amount
and frequency.
   Observations cited in connection with the Shwartzman phenomenon appeared to
substantiate the conception that the venom exerts its therapeutic effect by acting on
the capillaries and on the smaller blood vessels.   Clinical observations made during
the period of treatment of these patients further indicated that the cessation of bleed-
ing was due to the action of the snake venom and was not just a casual coincidence.

Lesions of the Cardiac Valve Rings in Rheumatic Fever.   L. GROSS AND C. K. FRIED-
     BERG.   Am. J. Path. 12: 4: 469, July 1936.
   The valve rings of 40 non-rheumatic control hearts and 97 rheumatic hearts were
studied.   The latter were divided into 6 clinical groups according to the presence

or absence of Aschoff bodies and the occurrence of one or more attacks of acute rheumatic fever. The valve ring is defined in detail. Roughly the term refers to the most proximal portion of the valve cusp excluding auricular myocardium. The normal rings rarely showed capillaries and never inflammatory cells. The rheumatic rings grossly showed a widening and irregularity in place of the usual fine sharp line of attachment. Microscopically, there were extensive inflammatory lesions which usually involved all of the valve rings. These consisted of extensive infiltration of inflammatory cells, vascularization, edema, scarring and, except in the last group, Aschoff bodies. These lesions usually involved all 4 rings, but the pulmonic ring was the most apt to be free. Fibroelastic reduplications were frequently present in the subaortic and subpulmonic angles, and there was frequently inflammation of the intervalvular fibrosa. The valve rings are stressed as strategic sites because it is believed that inflammation of the valves and neighboring sites occurs by spread from the rings.

Observations on Lymphogranuloma Venereum. B. A. KORNBLITH. Surg. Gynec. & Obst. 63: 99, July 1936.

A clinical pathological correlation is made of sixty cases in which the Frei intradermal reaction was found positive. The lesions reported fall into three distinct groups, (1) those involving the inguinal glands, (2) those involving the anus and rectum, (3) chronic genital lesions. The histopathology of the inguinal and pelvic glands removed at post mortem, and the tissue showing the Frei intradermal reaction are compared. A common histologic unit, the "micro epithelioid nodule," is stressed as the characteristic factor in identifying the disease in question. The use of the Frei antigen as a method of treatment is encouraging.

Coronary Artery Disease in Women. H. LEVY AND E. P. BOAS. J. A. M. A. 107: 97, July 1936.

In women under the age of 50, coronary artery disease is infrequent unless there is an associated arterial hypertension or diabetes mellitus. Of 169 women of all ages with coronary artery disease, only 7.7 per cent had neither arterial hypertension nor diabetes mellitus. The disease in women differs in no essential from that in men. The confusion arises from faulty interpretation of symptoms which in women are so often highly colored with secondary, functional symptoms. Precordial pain with or without radiation to the left arm, a sense of choking, and fear of death are common in the absence of organic heart disease.

Local Prophylactic Use of Antigas Gangrene Serum. H. LILIENTHAL. Ann. Surg. 104: 58, July 1936.

Musele is the principal tissue subject to infection by anaerobic organisms occurring in neighboring foci. Realizing from experience that serum or antitoxin intravenously administered does not act as a prophylactic, the author conceived the idea of applying gauze saturated with serum to the *uninfected* part of the wound made for draining an abscess of the lung. The abscess itself was treated primarily by packing, and outside the abscess a doughnut pad of this saturated gauze was applied as a packing of the chest wall, and left in place for several days. No infection of the chest wall followed in nine cases, and the same favorable effect was observed in a case of true gas gangrene of the leg.

The Clinical Aspects of Amyloidosis. E. MOSCHCOWITZ. Ann. Clin. Med. 10: 73, July 1936.

The chemical nature of the amyloid substance is not conclusively known. Pathologically, amyloidosis usually represents an involvement of the reticulo-endothelial

system and the pericapillary and periglandular connective tissue. Almost any tissue except the cerebrospinal substance may be involved, with a special predilection for the muscles and skin. In addition to the conventionally known causes, such as tuberculosis, chronic suppuration, syphilis, Hodgkin's disease and necrotizing blastomata, amyloidosis, either general or localized, is frequently associated with multiple myeloma and its attendant Bence-Jones proteinuria and with ulcerative lesions of the bowels. A case of amyloidosis associated with chronic deforming arthritis is reported. Such an association has been reported not infrequently, though the relationship is not clear. The number of reported cases of amyloidosis without apparent cause, in other words, primary amyloidosis, is progressively increasing and constitutes an important nosological entity. Experimentally, amyloidosis has been produced in various ways, but the underlying principle represents a prolonged overdosage with protein, preferably by the parenteral route. The evidences in favor of Letterer's contention that amyloidosis is the result of a hyperproteinemia and an associated hyperglobulinemia are reviewed and may be regarded as highly suggestive.

The clinical diagnosis of amyloidosis is dependent upon the following signs: (1) The enlargement of the viscera that may become palpable, namely the spleen and the liver. (2) The development of signs of the so-called nephrotic, but better termed hypoproteinemic syndrome consequent upon the involvement of the kidney. These are proteinuria, diminished blood proteins, hypercholesterinemia and generalized anasarca. In later stages, general arterial hypertension and azotemia may develop. The latter may occur without a coexisting hypertension, in contradistinction to other varieties of renal disease associated with hypertension. (3) Purpura of the skin. This sign has been less commonly observed but has been reported sufficiently frequently to be regarded as a symptom of the disease. (4) The Bennhold Congo red test forms the most important confirmatory test of amyloidosis. A 100 per cent retention of the dye is diagnostic.

There is abundant evidence that amyloidosis is clinically reversible; whether it is anatomically reversible has as yet not been definitely proved. Atypical amyloidosis constitutes a diverse variety of anatomical lesion. Clinically they may thus far be classified into four groups: (1) cases simulating scleroderma; (2) cases simulating myotonia; (3) cases simulating tumor of the tongue; (4) those associated with deforming arthritis.

Sigmund Freud—His Work and Influences. C. P. OBERNDORF. Am. J. Psychiat. 93:1, 21, July 1936.

This address was delivered before a joint session of the American Psychoanalytic Association and the American Psychiatric Association at St. Louis, Missouri on May 6, 1936, which marked the eightieth anniversary of the birth of Sigmund Freud. The speaker pointed out that while many men have received universal recognition during their life time, Freud is to be particularly felicitated in having attained the age of eighty in full mental and adequate physical vigor and in being the recipient of honors from the leaders of a great diversity of intellectual groups. After tracing briefly the factors which entered into the development of Freud's theory of psychoanalysis, the speaker grouped Freud's work into three periods—the first, the period of theory development (1885–1905); the second, the period of clinical research (1905–1920); and the third, the period of philosophical reflection (1920 to the present time).

The speaker emphasized that the elaboration of psychoanalytic theory has been almost exclusively the result of Freud's genius. Attention was called to the fact that the organization of psychoanalytic teaching and its standards had produced neither shortening of the process nor demonstrably better results in therapy. To be

sure, the increase in analysts, the extension of psychoanalytic theory and better preparation of the public for its use had widened its scope enormously. The current trends in psychoanalysis indicate two general categories—(1) tendency to extend and deepen metapsychological investigation and (2) further endeavor to adapt current theories to factual testing. The address closed with a tribute to the founder of psychoanalysis as "a simple man of science who recast much of the known wisdom of the ages in a form available for scientific application, who deepened this wisdom with his own genial additions and who fought with intrepid devotion for his convictions."

Biliary Duodenal Intubation. R. Colp. Surg. Gynec. & Obst. 63: 157, August 1936.

Biliary duodenal intubation has become a recognized and valuable surgical procedure in selected cases of certain primary diseases and as a secondary procedure in postoperative complications involving the extrahepatic bile ducts. It is indicated when the restoration of bile by internal drainage is imperative and the elimination of a biliary fistula is essential. It is exceedingly useful in reconstructive procedures of the bile ducts in which either an end-to-end anastomosis or a hepaticoduodenostomy, or choledochoduodenostomy is feasible. Its use is problematical, however, in those plastic procedures in which there is a loss of substance of the bile ducts and in which the indwelling tube is used as a temporary canal and scaffold along which a new tube of ductal epithelium may regenerate. It is still questionable whether bile duct epithelium will reform to any great extent. It is more than likely that the replacement will be made by connective tissue which will eventually contract, resulting in all probability in secondary strictures with bile stasis, ascending infection and cholangitis. Four cases involving this procedure are presented.

Gastro-Intestinal Bleeding in Diseases of the Liver and Biliary Tract. S. S. Lichtman. Am. J. Digest, Dis. & Nutrition 3: 439, August 1936.

The clinical findings in six patients suffering from gall-bladder or liver disease with gastro-intestinal bleeding as a complication are presented. Gross bleeding occurred in one case in the course of a degenerative liver disease. The blood was derived from congested necrotic areas in the liver and drained into the intestinal tract through the bile ducts. Massive bleeding may also occur in patients with cholelithiasis without jaundice. Laparotomy may disclose no source of bleeding. The cystic duct must remain patent to permit bleeding into the bowel. Cholecystectomy prevents recurrence of the bleeding. The types of gastro-intestinal bleeding occurring in the course of disease of the gall-bladder and liver have been classified. Distinction has been made between hemorrhages of local origin in the portal system, the liver parenchyma, the bile passages or the gastro-intestinal tract and those depending on a general hemorrhagic state secondary to jaundice and hepatic insufficiency.

Feeling of Unreality. C. P. Oberndorf. Arch. Neur. & Psychiat. 36: 322, August 1936.

The feeling of unreality is closely allied to the phenomenon of depersonalization and is in itself not a morbid entity. The distinguishing characteristic of the syndrome is the insight which the individual consistently retains regarding his abnormality. States of unreality are closely associated with thought block, feelings of stupidity, fugues, dream states and other types of involuntary withdrawal, of which loss of consciousness is the extreme state. A closely related syndrome is the severe dissociation of emotion from thinking. Psychoanalytically, this phenomenon represents an involuntary withdrawal from reality. Cases in which this symptom occurs are predominantly those of women.

The theory is advanced that thinking in certain individuals may in early life become associated with intellectuality either as a masculine or feminine characteristic. In such instances there occurs an identification of the patient with the parent of the opposite sex who happens to personify intellectuality to him. Invariably thinking in these individuals possesses definite erotic values. When something occurs in the reality situation which is incompatible with this ideal, repression and, subsequently, depersonalization symptom formation appear. The sequence of the mechanism in depersonalization may thus be stated: narcissistic wound caused by rebuff from the "stupid" parent, identification with the thinking parent; subsequent eroticization of thinking and repression of the eroticized thinking function as incompatible with the biologic rôle. These mechanisms are brought out in the illustrative case of a brilliant young man with whom thinking had become identified with a feminine father and activity with a masculine mother. Repression of the feminine component which the reality situation demanded put him in a helpless state, with the feeling of unreality as a predominating symptom of his psychic picture. Analysis of these unconscious factors enabled the patient to associate activity with masculinity and to dissociate intellectual endeavor from femininity.

Basal Metabolic Rate in Tuberculous Children. A. TOPPER AND H. ROSENBERG. Am. J. Dis. Child. 52: 266, August 1936.

A study of the basal metabolism of tuberculous children was made at Sea View Hospital. Of 115 patients with active, afebrile pulmonary tuberculosis of the adult type, 80 per cent had a normal basal metabolic rate. Of 143 patients with active, afebrile pulmonary tuberculosis of the childhood type, only 4.2 per cent had a normal metabolic rate. The rest, 95.8 per cent, had an increase in the basal metabolic rate (between plus 10 and plus 40 per cent). Reasons for this difference in metabolic response between patients with tuberculosis of the childhood type and patients with tuberculosis of the adult type are still theoretical, but the cause probably lies in the pathologic and immunologic differences inherent in the two types of infection.

Aural Manifestations of Lipoid Granulomatosis (Hand Schüller Christian's Disease). J. G. DRUSS. Ann. Otol. Rhin. and Laryng. 45: 3, 693, September 1936.

In the diseases which have been attributed to disturbances in lipoid metabolism, particularly Niemann-Pick, Gaucher, Hand Schüller Christian, the ear not infrequently shows clinical and pathologic manifestations. The clinical signs and symptoms are referable to the external ear, middle ear, mastoid, petrosa and their adnexa. Lesions in the mastoid produced by these diseases must be differentiated from the usual mastoiditis. Roentgen examination is of value in the differential diagnosis. The histopathologic changes in the temporal bone are in a general way quite similar to those in other flat bones of the body. A report is made of an interesting case of Hand Schüller Christian's Disease in which the temporal bone was sectioned serially.

Operation for Retention of an Artificial Eye after Exenteration of Orbit. I. GOLDSTEIN. Arch. Ophth. 16: 465, September 1936.

After a short review of the history of the operation of exenteration of the orbit, the author describes a plastic procedure permitting the retention of an artificial eye, which he devised to improve the cosmetic appearance. Ordinarily no support for such an eye is left following this deforming operation. The patient had had all the orbital contents including part of the lids removed for spindle cell sarcoma. The raw bone of the orbit was first covered with Thiersch grafts and the remainder of each lid placed against the bone. Six weeks later the lids were freed and the raw spaces

Thiersch grafted. Three weeks later the partially restored lids were split horizontally throughout their entire length forming in effect four lids. The raw surfaces of each sulcus were covered by Thiersch grafts fashioned about a dental mold. The artificial eye was later inserted in this sulcus between the split upper and lower lids. The article is illustrated with photographs.

Endocholedochal Section of the Sphincter of Oddi. R. Colp, H. Doubilet and I. Gerber. Arch. Surg. 33: 696, October 1936.

It has been shown by various investigators that certain aspects of the post cholecystectomy syndrome, acute pancreatitis and various forms of jaundice are apparently associated with spasm of the sphincter of Oddi. Attempts have been made in the past to section this sphincter through the transduodenal route. In this presentation the authors describe a new instrument designed to overcome the dangerous necessity of opening the duodenum. The instrument is passed down the common bile duct into the duodenum. The sphincter of Oddi is then sectioned with perfect safety and the instrument withdrawn. The operative results on thirty animals are presented. It is shown that the normal resistence of the canine sphincter of Oddi averages 150 mm. of water normally, and 300 mm. after spasm resulting from the local application of HCl. Six months after endocholedochal section of the sphincter, the resistance averages 90 mm. before and 110 mm. after application of HCl. This is indicative of marked reduction in function of the sphincter. In the absence of the gall-bladder, endocholedochal sphincterotomy is not followed by ascending infection.

Nonbacterial Thrombotic Endocarditis. Classification and General Description. L. Gross and C. K. Friedberg. Arch. Int. Med. 58: 620, October 1936.

In this paper the authors present a classification of endocarditis. They also present a study of forty-seven cases which were previously diagnosed as indeterminate, terminal or thrombotic endocarditis. These cases are now called nonbacterial thrombotic endocarditis. They are characterized anatomically by the occurrence of nonbacterial vegetations without appreciable reaction in the valve. An essential feature was the occurrence of these vegetations on valves which had almost invariably been the seat of previous disease (usually rheumatic). This form of endocarditis is viewed as an accidental occurrence in the course of any fatal disease, and is itself without any appreciable clinical significance. The cases are classified according to the clinical diseases in which they are found.

Nonbacterial Thrombotic Endocarditis. Associated with Acute Thrombocytopenic Purpura. C. K. Friedberg and L. Gross. Arch. Int. Med. 58: 641, October 1936.

In 3 cases, nonbacterial thrombotic endocarditis was associated with an acute fulminating (thrombocytopenic) purpura hemorrhagica. Clinically, the probability of a general infection was considered but blood cultures were sterile. In one of the cases there were widespread vascular lesions. A discussion is presented of the possible relationship of the vascular lesions to the development of the hemorrhagic phenomena.

Nonbacterial Thrombotic Endocarditis. Associated with Prolonged Fever, Arthritis, Inflammation of Serous Membranes and Widespread Vascular Lesions. C. K. Friedberg, L. Gross and K. Wallach. Arch. Int. Med. 58: 662, October 1936.

In 4 cases, the nonbacterial thrombotic endocarditis was associated with prolonged fever, polyarthritis, inflammation of serous membranes and a variety of vascular lesions. The differential diagnosis usually lay between a general infection, subacute bacterial endocarditis, rheumatic fever and tuberculosis. It was pointed

out that the symptoms in these cases resemble those of atypical verrucous endocarditis, but that the flat spreading variety of vegetation in that disease, as described by Libman and Sacks, was absent. It was suggested that these cases might also be related to those described by Baehr, Klemperer and Schifrin, and by Tremaine and Christian. The occurrence of nonbacterial thrombotic vegetations does not preclude the coexistence of some other associated valvular disease. In fact, its development probably depends on the existence of underlying disease in the valves.

Therapeusis of Problem Children. C. P. Oberndorf, S. Z. Orgel and Julia Goldman. Am. J. Orthopsychiat. 6: 4, 538, October 1936.

The authors review ten years of child guidance work at the Hebrew Sheltering Guardian Society's cottage-plan institution for dependent children at Pleasantville, New York where the number of children with psychoneurotic or psychopathic traits has risen gradually from approximately 15 per cent of the new admissions in 1925 to 68 per cent in 1935. A diagnostic grouping of the first fifty cases treated at the clinic for a period of one year or more disclosed a high frequency of psychoneurosis. This is due to the fact that conduct disorders, such as stealing, lying or persistent combativeness, were considered as the main presenting symptoms of obsessional acts. Several of the cases had previously proved troublesome in foster homes before their transfer to the institution and a considerable number had been actively treated for their conduct difficulties at other clinics and institutions. Despite grave misgivings as to the assimilability of the increased number of problem children, there has been no evidence of increased tendencies on the part of the normal children to imitate or adopt the undesirable proclivities of the problem child. Problem children have not been segregated. Indeed, it has been definitely determined that the presence in residence of as high as 40 per cent of problem children of both sexes, mingling freely, does not undermine the general morale of the institution.

Treatment at the clinic has been an eclectic procedure (embodying advice, consultation, persuasion, indulgence, temporization, privilege, change of environment from one cottage to another, toy technique, directed sublimatory activity in work, art and play). Physicians and members of the staff have used a psychoanalytic approach and availed themselves of inferences based upon psychoanalytic interpretations. All children on the clinic's roster were seen on the average for at least an hour every week. Frequency of visits and termination of treatment were determined by individual needs. Although the problem of estimating the worth of a therapeutic procedure is a difficult one, it was felt that at the end of ten years some attempt should be made to investigate the results of treatment. Accordingly, the subsequent adjustment of the first fifty children treated for one year or more was traced. These were children with conduct disorders of unusual severity. Follow-up revealed that five years or more after graduation eleven boys and fifteen girls were making their way satisfactorily; eight boys and six girls required only occasional assistance from our After-care Department; four boys and three girls had encountered serious difficulty; two boys were out of touch with the organization and one girl was dead. A graduate is considered to have adjusted himself well (1) when he has shown stability in useful employment; (2) when he has the ability to maintain himself; (3) when he has found it possible to adapt himself to his family and to his own circle, or when he has established a family of his own. As has been indicated, a goodly proportion has met these criteria. Aside from the benefits derived by the patient, the presence of the clinic in the institution has been a powerful influence in changing the attitude of both the teachers in the public school located on the grounds and the cottage mothers.

Effect of Moccasin Venom on Urinary Changes in Scarlet Fever. S. S. Schneierson, J. D. Lyttle and S. M. Peck. Am. J. Dis. Child. 52:796, October 1936.

Peck and Sobotka have shown that moccasin venom is capable of inhibiting the

Shwartzman Phenomenon. Lyttle has demonstrated by means of the Addis technique that in every case of scarlet fever there is a transient, explosive increase in the excretion of casts, proteins, red blood cells and white blood cells in the urine, from eight to forty-five days after the onset of the disease despite absence of clinical manifestations of nephritis: this he terms micronephritis. If the Phenomenon can be inhibited by the use of venom, then the possibility of inhibiting post-scarlatinal micronephritis, or even clinical nephritis by using venom seemed feasible, since there are many points of similarity between the vascular lesions of glomerulonephritis and the lesions of the Phenomenon.

Forty-two cases of scarlet fever at Willard Parker were studied. Twenty were used as controls and twenty-two were treated with venom in various doses. Daily Addis urinary counts were done on both groups. No appreciable differences were noted in both groups; micronephritis occurring about as frequently and as severely in both groups. No effect on the incidence of complications of scarlet fever, such as otitis media, adenitis, et cetera, were noted in the venom treated cases. Flexner and Noguchi showed that they could produce nephritis experimentally by the use of snake venom in toxic doses. This experiment illustrated, however, that moccasin venom in therapeutic doses did not cause any renal damage, even to kidneys that are more susceptible to injury.

Calcific Sclerosis of the Aortic Valve (Mönckeberg Type). A. SOHVAL AND L. GROSS. Arch. Path. 22: 477, October 1936.

The findings in 18 hearts with so-called Mönckeberg's calcific sclerosis of the aortic valve, in 19 hearts with a grossly polyvalvular extinct rheumatic process and in 13 hearts with a grossly monovalvular extinct rheumatic process are described. The essentially different gross and microscopic features of the Mönckeberg and rheumatic valvular lesions are noted. It is shown that the heart with the uncomplicated Mönckeberg process shows practically none of the stigmata of extinct rheumatic fever, and no other evidence which would indicate that the process is secondary to inflammatory changes. The possible mechanisms concerned in the development of the essential Mönckeberg process are discussed, from which it appears that this is purely and primarily degenerative, its occurrence and extent depending in all probability on individual predisposition to collagen involution and lipoid and calcium deposition. The findings in three hearts with submarginal aortic commissural bridging of non-inflammatory nature suggest that stress and strain in the aortic valve may serve as additional factors predisposing to degenerative processes. It is suggested that in certain persons in whom there exists a predisposition toward the deposition of lipoid and calcium, inflammatory lesions with subsequent deformity of the aortic valve may impose sufficient strain on the valve to initiate the Mönckeberg process.

Note on the Use of Evipal (N-Methylcyclohexenyl-methyl Barbituric Acid) in Coronary Occlusion. S. HIRSCH. Am. J. Med. Sci. 192: 5, 644, November 1936.

It is the consensus of medical opinion that relief from pain and absolute rest are essential in treating coronary occlusion; that somnolence for the first twenty-four to forty-eight hours or more after an acute closure is very desirable to eliminate the anxiety accompanying the severe precordial and arm pain. It is for patients who have not been relieved by the vasodilators, or the use of caffein sodiobenzoate and phlebotomy, that Evipal, as an intravenous anesthetic is recommended. A case is described wherein it proved a very valuable therapeutic agent when other measures failed.

Late Results in Acute Perforated Peptic Ulcer Treated by Simple Closure. M. A. SALLICK. Ann. Surg., 104, 5: 853, November 1936.

A study is presented of 74 consecutive cases of acute perforation of peptic ulcer treated by plication closure alone. The immediate postoperative mortality was 10.8 per cent.

Through combined special examination and replies to questionnaire, late study was obtained in 45 of the 66 patients who survived operation, giving recent information in 68.1 per cent of the cases. The follow-up period was over a 1 to 6 year interval; in most cases over 3 years had elapsed since operation. The author's criteria for evaluating late results are described in detail. Altogether, of the 45 cases followed, 29 were found to have significant further gastric complaints, a recurrence in this cries of 64.4 per cent.

These experiences indicate that acute perforation followed by successful closure results in permanent cure of ulcer in only a minority of cases; in almost two out of three cases peptic ulcer symptoms later recur. In most instances further medical or surgical care is required after recovery from acute ulcer perforation.

Differential Analysis of Bile Acids in Human Gall-Bladder Bile. R. COLP AND H.
DOUBILET. Arch. Surg. 33: 913, December 1936.

The gall-bladder bile in forty-five operative cases of chronic and acute cholecystitis and of carcinoma of the pancreas with obstruction, was analyzed for the following bile acids, (1) bile acids conjugated with taurine and with glycine; (2) cholic acid; (3) desoxycholic acid; (4) free bile acids.

Results. (1) In a number of cases in which the gall-bladder was found to be normal, analysis of the gall-bladder bile revealed the bile acids to consist of about 50 per cent cholic acid and 50 per cent non-cholic bile acids, mostly desoxycholic acid. The bile acids were conjugated to the extent of about 80 per cent, half with taurine and half with glycine. (2) In chronic cholecystitis, cholic acid formed about one-third of the total bile acids in gall-bladder bile. In acute cholecystitis, only about one-sixth of the total bile acids was cholic acid. (3) Free bile acids formed about one-third of the total bile acids in chronic cholecystitis and one-half in acute cholecystitis. (4) Bile acids are absorbed rapidly by the inflamed gall-bladder wall. This increased permeability is selective, the cholic acid being absorbed more readily than the desoxycholic acid, the glycine conjugated bile acids more quickly than the taurine bile acids, and the conjugated bile acids more readily than the free bile acids. (5) The fall in the relative percentage of cholic acid and the rise in the relative percentage of free bile acids apparently indicates that absorption of bile acids has taken place. (6) In two cases in which a pathologic condition of the liver was associated with a fairly normal gall-bladder, analysis of the gall-bladder bile revealed the proportions of the various bile acids to be similar to those formed in the bile of acute cholecystitis.

Cardiodynamic Relation to the Analysis of the Cardiac Contour. M. SUSSMAN. Am.
J. Roentgenol. 36: 6, 854. December 1936.

This review of the anatomy and the pathologic physiology of the ventricles has been given in an effort to make understandable the changes in the cardiac contour seen roentgenologically in various disease conditions. The changes in cardiodynamics depend on whether the cardiac musculature is healthy or diseased. When healthy, the response of the ventricle to an increased stroke output is dilatation of the outflow tract followed ultimately by hypertrophy of the outflow tract and of the inflow tract. The response of a ventricle to increased endocardiac pressure with small stroke output is hypertrophy without dilatation, manifested primarily in the inflow tract. In the presence of a diseased myocardium, the ventricle widens in outflow and inflow tracts. The degree of hypertrophy depends in a large measure upon whether a disturbance in cardiodynamics was present previously or not. These principles were

illustrated in an analysis of cases of Graves' disease, mitral disease, congenital cardiac disease, hypertension and myocardial disease.

It is believed that a knowledge of these principles will aid in the more useful interpretation of the cardiac contour. Such an analysis is also made necessary by the fact that so many cases do not conform to what the textbooks describe as "typical cardiac configurations."

A Vertical Microelectrophoresis Cell Employing Non-polarizable Electrodes. H. A. Abramson, L. S. Moyer, and A. Voet. J. Am. Chem. Soc. 58: 2362, 1936.

The horizontal electrophoresis cell has not been adapted to the measurement of particles which settle out of suspension. A vertical cell has been devised which embodies all of the characteristics of the one-piece glass cell described previously by Abramson and discussed more recently by Moyer. This vertical cell has been checked by comparing measurements on protein coated collodion particles, asbestos needles, and blood cells with measurements obtained in a calibrated horizontal cell. Agreement within the usual limits of experimental error was obtained. The advantages and disadvantages of the vertical cell are discussed. Preliminary data have been obtained on the electric charge of the giant ragweed pollen (Amb. trifida) in $M/150$ phosphate buffer $M/3$ glucose at pH 6.8.

Fever Therapy. W. Bierman. Arch. Phys. Therapy 18: 28, January 1937.

After a brief review of the history of fever therapy and of the report of physiologic changes occurring during temperature elevation, reference is made to the advantages of physically induced fever. An analysis of the therapeutic results obtained in the treatment of four hundred and sixty-two patients indicates that the disease of gonorrhea is the one which responds most dramatically to fever therapy whether the involvement be in the genito-urinary organs in both sexes or in the joints. A special technic yields brilliant results in the treatment of women. Other diseases favorably influenced are central nervous system syphilis, multiple sclerosis, chorea, and intractable asthma.

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CONTENTS

FELICITATIONS

The Journal of The Mount Sinai Hospital

pays tribute

to

DR. CARL KOLLER

CONSULTING OPHTHALMOLOGIST

and to

DR. BERNARD SACHS

CONSULTING NEUROLOGIST

in recognition of the great esteem in which they are held by their colleagues at The Mount Sinai Hospital for their notable achievements in the service of mankind.

It conveys to them, in this their eightieth year of life, the warm greetings and the sincere good wishes of their friends and associates.

THE WILLIAM HENRY WELCH LECTURES

ACETYLCHOLINE AS A CHEMICAL TRANSMITTER OF THE EFFECTS OF NERVE IMPULSES

I. History of Ideas and Evidence. Peripheral Autonomic Actions. Functional Nomenclature of Nerve Fibres[1]

SIR HENRY DALE

It is generally agreed that the excitatory process passing along a nerve or muscle fibre—what the late Keith Lucas (1910, 1912) called the "propagated disturbance"—is a self-propagating wave of reversible, physicochemical change. Its most easily recognizable manifestation is the discharge of an electrical potential difference, which is maintained between the inside and the outside of the fibre at rest. A theory which has found many supporters since the early days of modern physiology regards this electrical discharge as providing the actual mechanism of propagation, each point in succession being, on this theory, excited by the local current due to the depolarisation at the point just previously excited. For discussion of the history and details of this conception reference may appropriately be made to the writings of Ralph S. Lillie (1914, 1915, 1916, 1922, 1923), who has himself advanced highly suggestive evidence in favour of such a method of propagation, based on the analogy provided by the propagation of waves of "activation," over the surface of a metal rendered "passive" by a protective film of oxide. It may be supposed that the surface of a resting nerve axon forms a selectively impermeable film, the concentration of ions at which maintains the resting difference of potential, and that the nerve impulse, as it passes any point on the axon, temporarily destroys the selective properties of this film, thereby dissipating the concentration of ions and the consequent polarisation of the membrane, which are renewed as the excitatory process passes on and the resting condition is locally restored.

When special consideration has been given to the process by which the excitatory disturbance is transmitted across the slight anatomical discontinuity, at the ending of a nerve fibre in contact with an effector cell or the cell body of another neurone, it has usually, until quite recent years, been supposed to be essentially similar to that responsible for its propagation along the nerve. Kühne (1888) was possibly the first to suggest in definite terms that the muscle fibre, at its end plate, is electrically excited

[1] Delivered at The Blumenthal Auditorium, The Mount Sinai Hospital, New York City, May 7, 1937.

by the arrival of the potential change of the nerve impulse at the asymmetrical branchings of the nerve fibre, where it terminates in contact with the end plate. The fact that the wave of electrical change accompanying activity in muscle is capable of giving rise to a derived current of sufficient intensity to act as a stimulus, has been familiar since the early experiments of Mattencci and Du Bois Reymond on the excitation of a frog's nerve by action currents in a muscle or heart of the same species. Kühne (loc. cit.) further demonstrated that, if the overlapping ends of two sartorius muscles from a frog were fixed in intimate contact by a suitable clamp, a wave of excitation in one was transmitted by the action current to the other, so that the wave of contraction passed along the two muscles almost as though they were one. Since, however, the normal direction of physiological transmission is from nerve to muscle, it should be noted that transmission by the excitatory effect of the electrical change has thus been demonstrated artificially from muscle to nerve, or from muscle to muscle, but never from nerve to muscle. This contrast could, in itself, obviously be explained on quantitative lines; indeed, if the weak potential change accompanying an impulse in a single nerve fibre were capable of exciting even contiguous fibres in the same nerve, under physiological conditions, no selective transmission of stimuli would be possible. It could properly be argued, moreover, that the stimulating effect of a current derived from naked nerve endings, in intimate contact with the naked protoplasm of a muscle end plate, could not be imitated by the variations occurring in a whole nerve laid on the surface of an intact muscle. At one point, however, such reasoning appears to me to encounter a serious difficulty. If we assume that the intimacy of contact, at the nerve ending on an end plate, affords sufficiently favourable conditions for the transmission of the excitatory process from the one to the other by the stimulating effect of the electrical variation, it is very difficult to understand why such transmission should be irreciprocal; why an impulse passing down a nerve fibre and reaching the ending should so readily start a wave of excitation, and consequent contraction, in the muscle fibre, while the passage of a wave of excitation along the muscle fibre entirely fails to excite the nerve fibre at its ending. In support of an electrical explanation of a transmission so definitely irreciprocal in the direction nerve → muscle, it is hardly legitimate to cite experimental demonstrations of such transmission by artificial contact, when these only succeed in the direction muscle → nerve. To make the electrical theory of propagation fit the conditions of transmission between nerve ending and effector cell or secondary neurone, and especially its rigidly irreciprocal nature, it needs at least to be complicated by subsidiary hypotheses.

Nevertheless, until quite recent years the electrical theory of the propagation of excitation, not only within the limits of the individual neurone or muscle fibre, but across synaptic and myoneural junctions, practically

held the field.   It is the more interesting to note that Du Bois-Reymond (1877) had already considered the different possibility, that the excitation of a muscle fibre through a nerve fibre might be due to the release of a chemical stimulant, when the impulse arrived at the nerve ending.   Writing of the transmission from motor nerve to voluntary muscle fibre, he states (loc. cit. p. 700):

"Von bekannten Naturprocessen, welche nun noch die Erregung vermitteln könnten, kommen, soviel ich sehe, in Frage nur zwei.   Entweder müsste an der Grenze der contractilen Substanz eine reizende Secretion, in Gestalt etwa einer dünnen Schicht von Ammoniak oder Milchsäure oder einem anderen, den Muskel heftig erregenden Stoffe stattfinden.   Oder die Wirkung müsste elektrisch sein."

The rest of the chapter, in which this alternative is stated, suggests that the author, at that time, regarded the chemical transmission theory as, on the whole, the more likely of the two.   Such speculations, however, had no effect on the course of general opinion, and this alternative to the electrical theory was not seriously considered until Loewi (1921) demonstrated that the effects of the vagus and sympathetic nerves on the frog's heart were indeed produced by the liberation, at their respective endings, of chemical substances which specifically inhibited and augmented its activity.   Writing in 1933 of the transmission of excitation from motor nerve ending to striated muscle fibre, Adrian (1933) considered the possibility of a chemical mechanism even in this case, analogous to that which Loewi had demonstrated twelve years earlier for the heart vagus, as well as the more conventional electrical theory.   "It is by no means certain," wrote Adrian, "that the humoral transmission of the vagal effect differs in kind from the transmission of activity from motor nerve to striated muscle.   An exciting substance liberated at a nerve ending but destroyed within a few thousandths of a second would have little chance of spreading by diffusion and would account well enough for the known properties of the nerve ending.   It is equally likely that the more direct kinds of transmission depend, as in nerve fibre, on electric forces disturbing the balanced reactions of surface membranes."

Adrian's statement was at least a year in advance of any experimental evidence clearly in favour of a chemical transmission of excitation from motor nerve to voluntary muscle.   His own work, of course, had largely been concerned with the study of nerve impulses by physical methods; and it is interesting to contrast his readiness for this extension of the chemical mechanism, with the reluctant caution of Otto Loewi (1933), the first to demonstrate such a mechanism elsewhere, who in that same year stated in a lecture, given here in New York: "Personally I do not believe in a humoral mechanism existing in the case of striated muscle."

My aim, in these lectures, will be to put before you the evidence for such a mechanism, at all synaptic or cytoneural junctions connected with the peripheral nervous system.   A full historical review would, I think,

have to trace the evidence, in which such a conception originated, at least
as far back as the closing decade of the nineteenth century, when Langley
and Anderson were unravelling the tangle of the involuntary or autonomic
nervous system, and Schafer and his co-workers, testing the immediate
effects of injecting extracts of various glands and organs, came across the
remarkable active principle of the suprarenal medulla (Oliver and Schafer,
1895), and found that the other organs tested, with one exception, yielded
vasodepressor extracts of varying potency.   A link between these appar-
ently unrelated, though contemporaneous, sets of investigations was
found, when Lewandowsky (1899), Langley (1901), and finally Elliott
(1905) showed the remarkable correspondence between the actions of
epinephrine (adrenaline) over a wide range of organs and species, and those
produced on the same organs by nerves of the true sympathetic, as dis-
tinguished from the parasympathetic division of the autonomic system.
The real clue to this truly astonishing correspondence was actually given
in a suggestion by Elliott (1904), far in advance of its time.   "Adrenaline,"
he wrote, "might be the chemical stimulant liberated on each occasion
when the sympathetic impulse arrives at the periphery;" a clear prevision
of the process of chemical transmission as we know it to-day.   There
were few who regarded Elliott's suggestion seriously; apparently he did not
carry it forward into his own main paper (1905) on this subject.   Dixon
(1906, 1907), however, adopted it and extended it, by analogy, to the para-
sympathetic vagus nerve, even claiming to have detected the liberation in
the dog's heart of something like muscarine, as the result of vagus stimula-
tion.   If Reid Hunt (1906) had examined more in detail the action of
acetylcholine, the intense depressor activity of which he described in
Toronto, actually at the same meeting as heard Dixon's (1906) first descrip-
tion of his vagus experiments, I think it must have been realized that
acetylcholine would be a more suitable and likely parasympathetic trans-
mitter than muscarine.   Actually, such a detailed study was not made till
eight years later, when I came across acetylcholine in another connexion
(Dale, 1914).   I was led to make a direct comparison, between the re-
production of parasympathetic nerve effects by the remarkably brief
actions of acetylcholine, and the already long-recognised reproduction of
sympathetic effects by the rather less rapidly evanescent actions of epi-
nephrine, each reproducing, as I pointed out, "those effects of involuntary
nerves which are absent from the action of the other, so that the two
actions are in many directions complementary and antagonistic."   I
ventured no further, however, than to suggest that these correspondences
gave "plenty of scope for speculation."   I further observed that when this
intense parasympathomimetic activity, this "muscarine" action of acetyl-
choline, as I termed it for brevity, was abolished by atropine, another
type of action came to light, in which it closely resembled nicotine as a
stimulant of all ganglion cells, and at least of some voluntary muscles.

This action, at the time of its discovery, suggested nothing more than a vaguely conceived "biochemical similarity" between these structures and the effector units innervated by parasympathetic nerves. Its true and remarkable significance will appear in the later part of these lectures.

Such was the position in 1914. Two substances were known, with actions very suggestively reproducing those of the two main divisions of the autonomic system; both, for different reasons, were very unstable in the body, and their actions were in consequence of a fleeting character; and one of them was already known to occur as a natural hormone. These properties would fit them very precisely to act as mediators of the effects of autonomic impulses to effector cells, if there were any acceptable evidence of their liberation at the nerve endings. The actors were named, and their parts allotted; a preliminary hint of the plot had, indeed, been given ten years earlier, and almost forgotten; but only direct and unequivocal evidence could ring up the curtain, and this was not to come till 1921.

It was in the latter year that Otto Loewi (1921, 1924, 1926) began to publish a series of papers, giving the direct experimental evidence of the humoral or chemical transmission of the excitatory (or inhibitory) process, from the endings of vagus and sympathetic nerve fibres to the heart muscle of the frog. The experiments had a classical directness and simplicity. The washed heart, suspended from a Straub cannula, held a small quantity of Ringer's solution. When the appropriate nerve was effectively stimulated, this solution acquired the property, when removed and transferred to a second, control heart, of reproducing in this the effect of the nerve stimulation on the first, whether inhibition by vagus or acceleration by sympathetic impulses. Others, who repeated and confirmed these observations, produced some refinements of method. Thus, Kahn (1926) suspended both hearts from a common cannula with two necks, so that the beating kept their contents mixed, and showed that stimulating the nerve, to one only, produced the specific effect in both. Bain (1933) later achieved the same result by a steady perfusion, passing first through the stimulated or donor heart and then to the control or recipient. Brinkman and van Dam (1922) had shown that the fluid from a frog's heart under vagus stimulation caused not only inhibition of another heart, but contraction of a frog's stomach, through the vessels of which it was perfused; it possessed, accordingly, an activity corresponding not merely to that of the heart vagus, but to that of vagus or parasympathetic nerve fibres in general.

Meanwhile the experiments of Loewi and his co-worker Navratil were throwing light on the nature of the transmitters and on the manner of their intervention. The transmitter of vagus inhibition was early revealed as an unstable ester of choline; such properties, indeed, as could be tested on the minute scale to which the experiments were restricted, were

indistinguishable from those of acetylcholine. Its activity could be destroyed by mild hydrolysis with alkali, and restored to even more than the original strength by acetylation—the excess being easily accounted for by the presence of some free choline in the fluid, as originally tested. A point of fundamental importance was established, when it was found that atropine, in abolishing the effect of vagus stimulation on the heart, did not interfere with the liberation of the vagus substance, but only prevented its inhibitory action; and that similarly ergotoxine or ergotamine did not prevent the liberation of the sympathetic transmitter, but only interfered with its accelerator and augmentor effects on the heart muscle. Loewi was early able to demonstrate the presence in heart muscle of an esterase, destroying by hydrolysis the activity of his vagus substance, which could be restored by acetylation; just as I had assumed the hydrolysis of acetylcholine by an esterase to account for its evanescent action and its rapid disappearance from the circulating blood. Later it was shown by Engelhart and Loewi (1930) and by Matthes (1930) that the rapid destruction of acetylcholine in shed blood, which Galehr and Plattner (1928) had demonstrated, is due to the presence of the esterase; and work in more recent years, particularly by the Stedmans, has shown that the enzyme concerned is not an ordinary lipase, but a cholinesterase, specifically and intensely active on unstable choline esters, such as acetylcholine. It had long been recognized that eserine specifically increased the excitability of the heart, the salivary gland, or the bladder to parasympathetic nerve impulses. Loewi and Navratil (1926) showed that this potentiating action of eserine, on the response of the heart to vagus impulses, was due to its inhibiting the action of the esterase, and protecting the vagus substance from its destructive effect.

This demonstration of the nature of the eserine action has been of the greatest value, especially in extending the investigation to mammals, in which the blood usually contains a highly active amount of cholinesterase, and where even with saline perfusions, at the natural warmth necessary for activity of the organs, little or none of the parasympathetic transmitter escapes destruction by the tissue esterase, unless eserine is present. Under such conditions, the direct potentiation of a nervous effect by eserine afforded, by itself, a presumption that the effect was being transmitted by the release of the transmitter which Loewi had called the "vagus-substance." I think that Gaddum and I (1930) were probably the first to use eserine for this kind of diagnostic effect, in our investigation of the so-called Vulpian pseudo-contraction of the denervated tongue. Eserine gave us evidence that the phenomenon was due to an unstable choline-ester, presumably acetylcholine, released at the endings of *chorda tympani* fibres to transmit their vasodilator action, some of it escaping on to the voluntary muscle fibres, rendered sensitive to it by denervation. On the same organ, the dog's tongue, eserine was later used by Feldberg to enable

him to catch the transmitter of *chorda tympani* effects in the venous blood, during stimulation of the nerve, and to study its various physiological effects, such as its action on the muscle of the body wall of the leech, and its vasodilator action in the cat; with the result that he found it to correspond in all its properties and actions with acetylcholine.

The evidence for the nature of the sympathetic transmitter came more slowly. It was natural, of course, from the first to think of epinephrine. Cannon and his co-workers in the Harvard laboratory, who had found that stimulation of certain sympathetic nerves caused the escape into the blood of something which would produce sympathetic effects on distant organs, referred to it as "sympathin." In recent years they have obtained evidence (cf. Cannon, 1933) which convinces them that the effects produced by "sympathin," when thus carried by the blood, are in the direction of augmentation or inhibition, according to the effect of the nerve stimulation which caused its release. They believe, accordingly, that "sympathin," in producing its effect, enters into combination with a receptive substance which determines the sense of its action, and that it is in this combined form that it escapes into the circulation. If these views are accepted, the essential transmitter, as released at the nerve endings, should be a substance capable of producing either an augmenting or an inhibiting effect, according to the nature of the receptive substance which it meets in the effector cells; and on those lines it might well be epinephrine itself. So far as it has been examined, when existing free in watery media, such as the aqueous humour of the eye or Ringer's solution, the chemical properties, demonstrated by Bacq (1933), and most recently and convincingly by Loewi (1936), are entirely in favour of its being, indeed, epinephrine. The final decision on this point, however, must be left to those who are directly concerned with its investigation.

Returning to the question of Loewi's vagus substance, the transmitter of peripheral parasympathetic effects, we have seen that there was plenty of evidence to suggest that it was a choline ester, of properties very similar to those of acetylcholine. There were sufficient reasons, however, against too ready an assumption as to its identity. There was no evidence at that time that any choline ester occurred as a constituent of the normal animal body, and this was not obtained till 1929, when my late colleague Dudley and I (Dale and Dudley, 1929) found evidence for the presence of such an ester in extracts from the spleens of horses and oxen. Dudley was able to isolate and to identify it chemically as acetylcholine, and no other simple ester of choline was found, or has yet been found, to occur thus naturally. The presumption thus became very strong that the substance liberated by nerve impulses in animal tissues, and having the properties of acetylcholine, was that ester, and no other. A difficulty of a different kind was presented by the action of atropine. All the actions of acetylcholine in which it reproduced the peripheral actions of parasympathetic nerves—

all its so-called muscarine actions—were very readily annulled by a small dose of atropine; but of the corresponding effects of parasympathetic nerves, only some were similarly liable. There seemed to be no rule about it; and, indeed, there is no sharp contrast between parasympathetic effects liable to atropine and those indifferent to it, but a graded series. The inhibitor effect of the vagus on the heart, for example, is more readily suppressed by atropine than is its motor effect on the stomach; and this, again, is more sensitive to atropine than is the effect of the same nerve on the small intestine. All these parasympathetic effects, even the most resistant to atropine, were greatly intensified by eserine; and we have seen that a large potentiation by eserine is, by itself, an indication that an unstable ester of choline is concerned. Nor was it possible in any degree to lessen the difficulty created by this varying influence of atropine, by suggesting that some other ester than acetylcholine was acting as transmitter; the actions of all of them, and even of choline itself, appear to be equally liable to annulment by atropine.

Apparently there was a conflict between the evidence of eserine, in favour of an unstable choline ester, like acetylcholine, as the mediator, and the evidence of atropine against it. The difficulty, however, soon took another form. For it was not only in connexion with the atropine-sensitive nervous effects, such as the action of the third cranial nerve on the pupil (Engelhart, 1931), or of the *chorda tympani* on the salivary secretion (Babkin, Stavraky and Alley, 1932; Henderson and Roepke, 1933; Gibbs and Szelöczey, 1932), that the liberation of a substance having all the properties of acetylcholine could be detected. A substance of exactly the same characteristics was demonstrated with equal ease in the venous blood (Feldberg, 1933) or perfusion fluid (Bain, 1933, 1936) leaving the blood vessels of the dog's tongue during the vasodilator action of the *chorda tympani*, although this effect was apparently indifferent to atropine. Similarly Feldberg and I (1934a.) found that the contraction of the musculature of a dog's stomach in response to vagus stimulation, also resistant to atropine, though less completely so, was accompanied by the appearance of the same substance in the venous blood, or perfusion fluid, leaving the gastric veins; and we were able to obtain it in sufficient quantity to compare it with acetylcholine in unusual detail, with the result that we concluded, with some confidence, that it was acetylcholine itself. The evidence that these atropine-resistant nervous effects were transmitted to the effector cells by the liberation of acetylcholine, was, indeed, quite as good as for the atropine-sensitive effects.

How then were we to explain the fact that atropine interfered hardly at all with the effects of the nerve impulses, but easily annulled those of the substance transmitting them, when we obtained this in solution and applied it artificially? Gaddum and I (1930) had offered an explanation of a similar anomaly, in connexion with the Vulpian pseudocontracture;

and it still seems to me to be adequate. We suggested—and the descriptions of histologists support the suggestion—that the endings of autonomic nerve fibres may show a widely varying intimacy of relation to the effector cells; some endings being outside the cell at some distance from its surface, others in close contact, others again, if we accept the histological evidence, inside the cell membrane, in the cytoplasm. It is surely not difficult to suppose that an effect of acetylcholine reaching the effector cell by diffusion, from the blood vessels when it is artificially injected, or from nerve endings outside the cell when it is liberated at these, may easily be prevented by atropine; but that this antagonist cannot similarly intervene, when acetylcholine is liberated from nerve endings in immediate contact with, or even inside the cell membrane.

Thus steadily, by cumulative evidence, Loewi's fundamental discovery was extended from the frog's heart vagus to the whole parasympathetic system in mammals; and the substance concerned in transmitting the excitatory effect, from the peripheral endings of these nerves to the effector cells, was identified with an increasing confidence as acetylcholine. The substance similarly responsible for transmitting the excitatory effect from the peripheral endings of most nerves of the sympathetic system, though not yet so completely identified, was, by general consent, allied to epinephrine. There were certain exceptions, however, to the general correspondence between the effects of sympathetic nerves and those of epinephrine, some of them long recognised as anomalies. Dastre and Morat (1884), for example, had long ago observed that stimulation of the cervical sympathetic nerve caused vasodilatation in the mucous membrane lining the inner surface of the lips and cheeks of the dog; and Elliott (1905) had looked, without success, for a reproduction of this effect by epinephrine. Rogowicz (1885) showed that this effect, like that of the *chorda tympani* on the denervated tongue, was accompanied by contracture of the neighbouring voluntary muscles of the lips and cheek, if these had been denervated by section of the facial nerve. The resemblance to the pseudocontraction of Vulpian was very suggestive, and Von Euler and Gaddum (1931), in my laboratory, found that the effect described by Rogowicz was, indeed, potentiated by eserine. The evidence led to the suggestion that there were fibres in the dog's cervical sympathetic nerve, belonging to the true sympathetic system, but transmitting their effects by peripheral liberation of acetylcholine, after the manner of parasympathetic nerves. A better known case is that of the sweat glands. It has long been recognised as an anomaly that, although their nerve supply is entirely from nerves belonging to the true sympathetic system, the secretory activity of these glands, in the cat and in man, is stimulated by pilocarpine, or by eserine, and paralysed by atropine, while it remains practically unaffected by epinephrine or by the paralytic action of ergotoxine. The suggestion now became obvious that the sympathetic nerve

fibres to these glands transmit their effects by liberating, not epinephrine or anything like it, but acetylcholine; and Feldberg and I (1934b.) were able to obtain direct evidence by perfusing the foot of a cat with Locke's solution containing eserine, and showing that, when the sympathetic nerve supply was stimulated, acetylcholine appeared in the venous effluent, provided that the perfusion included the hairless pads, to which the sweat glands are limited; but that no acetylcholine was produced by the same stimulation, when the pads were excluded from perfusion by ligature. The general statement that parasympathetic nerves transmit their effects by liberating acetylcholine, sympathetic nerves by liberating epinephrine or something closely related to it, though it truly represented a broad distinction, was evidently not without exceptions.

Precision and convenience seemed, therefore, to demand a nomenclature enabling us to refer to a nerve fibre or impulse in terms of the chemical transmitter of its activity to the effector cell, irrespective of its anatomical origin. I proposed (Dale, 1933), accordingly to differentiate "cholinergic" and "adrenergic" fibres or impulses, and the words seem to have been useful. Bülbring and Burn (1935) have observed that the sympathetic nerves to the blood vessels of the leg muscles, in the dog, contain vasodilator fibres which are cholinergic, and, according to Bacq (1935, a & b), the fibres in the hypogastric nerve of the dog supplying the blood vessels of the penis, though purely sympathetic, are mostly cholinergic. Bacq and Fredericq (1934) have detected a cholinergic component in the sympathetic fibres which innervate the plain muscle of the orbit, causing retraction of the nictitating membrane in the cat. On the other hand the vagus has been shown to contain fibres, which appear to belong intrinsically to it, and therefore to be parasympathetic in origin, which cause acceleration of the heart and inhibition of the stomach, when the normally predominant vagus effects have been eliminated by atropine; and the *nervus erigens*, purely parasympathetic and predominantly cholinergic, has been shown to contain fibres, joining it by a separate, slender root, the stimulation of which causes vasoconstriction. It may be suspected that these represent cases of parasympathetic nerve fibres which are adrenergic in function. There is evidence (J. Z. Young, 1932) that in certain fishes the familiar association between the two types of chemical transmission and the two divisions of the autonomic system may even be reversed, the effects of the sympathetic nerve supply to the iris of *Uranoscopus* corresponding to those of acetylcholine, while those of the third cranial nerve correspond to those of epinephrine. When once it is thus realized that the chemical functions of the post-ganglionic fibres of the autonomic system do not, even in the mammals, correspond exactly with their anatomical connexions, the position is greatly simplified.

It is to be noted that there is no evidence here to suggest the existence of more than the two recognized chemical transmitters; whenever the

chemical function of a fibre arising from an autonomic ganglion has been determined at all, it has been found to be either cholinergic or adrenergic. There are, however, still certain additional questions to be answered. Accepting the evidence that acetylcholine is liberated to transmit the stimulus from the ending of a cholinergic fibre, we ought to enquire whether it can perform that function by itself, or whether there is evidence of something else liberated with it, and required in addition for the transmission process. The question is raised in definite form by the early experiments of Howell (1906, 1908), who, some fifteen years before Loewi's experiments, showed that potassium ions were liberated in the perfused heart when the vagus nerve was stimulated. Howell, however, did not, according to my reading of his publications, suggest that the potassium ions were liberated at the vagus endings, to convey the inhibitory stimulus from them to the heart muscle. The most recent evidence makes it clear, in any case, that the potassium ions come from the heart muscle fibres, as a part of the change effected in them by the inhibitory stimulus, transmitted by acetylcholine. Prof. Lehnartz, of Göttingen, recently showed, in my laboratory, that the liberation of potassium ions, from a tortoise auricle, is caused by the artificial application of acetylcholine just as by vagus stimulation; but by neither if the inhibitory effect is prevented by atropine. In this case, accordingly, and by analogy in others, we may conclude that the essential transmission of the stimulus from nerve endings to effector cells is performed by acetylcholine alone. Similarly, there is no reason to suppose that the sympathetic transmitter, epinephrine or a nearly related substance, requires the co-operation of any other substance in performing its essential function.

There is another question of greater importance for my main theme. Accepting the evidence that nerve fibres arising from autonomic ganglia, so far as the chemical transmission of their effects is known, are either cholinergic or adrenergic, we still have to enquire whether the effects of all such fibres are chemically transmitted, or whether, even here, there is evidence also of a direct, physical transmission of excitation, as an alternative or supplementary mechanism. We have considered earlier the difficulties presented by the effects of certain apparently cholinergic nerves, persisting when the corresponding effects of acetylcholine have been annulled by atropine. Long ago I pointed out that, in many cases, the augmentor effects of stimulating sympathetic nerves—effects of adrenergic impulses we should now call them—were much more resistant to the paralysing action of ergotoxine than the corresponding effects of epinephrine, reaching the effector cells through the circulation. Two cases of this kind of discrepancy have attracted special attention in recent years. Henderson and Roepke (1934) call attention to the fact that the response of the urinary bladder to stimulation of its parasympathetic nerve supply in the pelvic nerve shows a quick, contractile and a slow, tonic phase.

Acetylcholine, in ordinary doses, produces an effect corresponding to the tonic phase only; and only this phase of the response to nerve stimulation is sensitive to the effect of atropine.   They conclude that the quick response is produced by some other mechanism of transmission.   Similarly Monnier and Bacq (1934, 1935), recording the retraction of the nictitating membrane in the cat, find that stimulation of the sympathetic nerve supply causes a quick, followed by a slow, sustained effect.   Only the latter is reproduced by injecting epinephrine, and only this slow phase, whether produced by epinephrine or by nerve impulses, is weakened or suppressed by the synthetic dioxane known as 933 F, which leaves the quick response to nerve impulses relatively unaffected, or even, in some cases, apparently enhanced.   Monnier and Bacq give other evidence that the effect of 933 F is to quicken the contraction of the plain muscle moving the nictitating membrane, so that it becomes less like the slow increase of tonus characteristic of plain muscle, and more like the quick twitch of striated muscle.   They conclude that, in addition to the normally predominant, adrenergic effect of the sympathetic nerve impulses acting on this muscle, there is a subsidiary mechanism by which the physico-chemical disturbance, constituting the nerve impulse, is directly transmitted to the plain muscle fibres without the intervention of a chemical transmitter; and that this physically transmitted excitation is responsible for the quick phase of the retraction, and is naturally unaffected by the suppression of the response to epinephrine.   Eccles's experiments on the electrical changes in the nictitating membrane lead him to a similar point of view.

You will observe here the intrusion of an idea that, although the chemical transmission may be adequate for the production of slow and long-persistent responses, a quick response requires a fundamentally different, physical transmission of the excitatory process from nerve ending to effector cell.   A plausible scheme could, indeed, be made on those lines. We might regard as the primitive arrangement a separation of the effector cells by a significant interval from the nerve endings, from which the chemical transmitter, liberated by the arrival of impulses, would reach the effector cells by relatively slow diffusion.   Observations, such as those of G. H. Parker (1936), on the nervous control of the chromatophores in the skins of certain fishes by 'neurohumors' would justify this conception. We might then suppose that, in the course of evolution, when a quicker form of response is required, this chemical transmission is supplemented by a direct, physical transmission of the excitation wave, from nerve endings which make a close contact with the quickly reacting effector cells. The same experimental facts could, however, be interpreted in a different manner.   We might regard the approach of the nerve endings to the effector cells as merely enabling the chemical transmitter to be released in closer and closer contact with these.   When an impulse arrived at a nerve ending which made direct contact with or was even internal to the surface

of an effector cell, the concentration of the chemical transmitter would there rise with great abruptness, producing a quick reaction, and one relatively insusceptible to antagonistic drugs. We might then reasonably suppose that the transmitter, whether it was thus released in close contact with cells immediately innervated, or from freer nerve endings, would reach other cells more slowly, by diffusion from these sites of its liberation. We thus obtain, I think, at least a plausible alternative conception of the meaning of these two-phase reactions to nerve stimulation, and of the similarity of their slow phases to the effects of acetylcholine and epinephrine artificially injected, which does not involve the introduction of a second, purely physical neuromuscular transmission.

Our choice between the two interpretations must depend, I think, on our readiness to consider the possibility of a chemical method of transmitting the excitation, even for such quick and individual reactions as the twitch of a voluntary muscle fibre, in response to a motor nerve impulse, or the discharge of a postganglionic nerve impulse from a ganglion cell, on the arrival of a preganglionic impulse at the synapse. It will be the aim of my second lecture to put before you a body of direct evidence which seems to me not merely to justify, but even to necessitate the consideration of these possibilities.

Meanwhile I would ask your attention to evidence concerning the method of neuromuscular transmission in certain intermediate cases. In these, layers composed of cross-striated muscle fibres, relatively quick in contraction, replace the layers of plain muscle found in the analogous organs of other animal types; but these striated muscle fibres are innervated by parasympathetic nerves, and their activities are not, in the full sense, under voluntary control. The sphincter of the bird's iris is a longknown example. It is innervated from the third cranial nerve, and its relatively quick response to nerve impulses is unaffected by atropine, but readily abolished by curare. In these respects it seems to behave like a voluntary, striated muscle. We find, however, that it is caused to contract by choline esters, including acetylcholine, but not by natural muscarine, which causes intense constriction of the mammalian pupil. We find also that these actions of choline esters on the bird's pupil are annulled by curare and not by atropine; so that the effect on it of choline esters, and of acetylcholine in particular, belongs to the nicotine action and not to the muscarine action of these compounds. An even more striking example is provided by the muscular wall of the intestine of the tench, which, as Mehes and Wolsky (1932) have shown, has two distinct layers, the outer consisting of striated, the inner of plain muscle fibres, both alike being innervated by the vagus. In this case, a quick reaction of the outer, striated layer precedes a slowly developed tonus and rhythm of the inner, plain muscle layer, when the vagus is subjected to faradic stimulation. Exactly the same sequence is observed when acetylcholine is artificially

applied to an isolated preparation of this intestine; and curare selectively paralyses the reaction of the striated coat, atropine that of the plain muscle coat, to either kind of stimulus. Here, then, we have two examples, in which there can be no reasonable doubt that acetylcholine is acting as the chemical transmitter of excitation from parasympathetic nerve endings to striated muscle fibres, on which its excitatory action is of the "nicotine" type, being unaffected by atropine and readily paralysed by curare. The nicotine action of acetylcholine, accordingly, has a physiological significance. It is obvious that such a conclusion may have very far-reaching implications; and these will be the subject of my second lecture.

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ACETYLCHOLINE AS A CHEMICAL TRANSMITTER OF THE
EFFECTS OF NERVE IMPULSES

II. Chemical Transmission at Ganglionic Synapses and Voluntary
Motor Nerve Endings. Some General Considerations[1]

sir henry dale

Hitherto we have been dealing with the transmission of the excitatory
process, from nerve endings to effector cells, in cases where the intervention
of a chemical transmitter, or mediator, presents no serious difficulty of
conception. We have considered, as yet, only transmission from the end-
ings of postganglionic fibres of the autonomic system, to involuntary
muscle or gland cells. So far as the cholinergic nerve fibres of this type
are concerned, the responses evoked from the effector cells have belonged
almost entirely to what we have called the 'muscarine' aspect of the action
of acetylcholine, and they have been chiefly concerned with the augmenta-
tion or inhibition of spontaneous activities. Such effects have a long
latency, rise slowly to a maximum with repetitive stimulation of the nerve,
and sensibly outlast the period of such stimulation. It is not at all diffi-
cult to picture them as produced by the liberation of a chemical mediator
at the nerve endings. And the same applies to those few examples which
we have hitherto noted, of the transmission of excitation from parasympa-
thetic nerve endings to certain striated muscle fibres by acetylcholine,
acting there by virtue of its 'nicotine' action; in these cases also we are
concerned with reactions to repetitive stimulation of the nerve, quicker,
indeed, than those of unstriated muscle, but very slow and persistent in
comparison with a twitch of a voluntary muscle.

The question was insistent, however, whether the very striking stimulant
effects of acetylcholine on ganglion cells and on certain voluntary muscles,
which we had referred collectively to its 'nicotine' action, had no physio-
logical meaning, except for these aberrant cases of striated muscle fibres
with parasympathetic innervation. It was difficult to suppose that
ganglion cells and voluntary muscle fibres would be endowed with this
sensitiveness to acetylcholine, if the only physiological function of the
latter were the transmission of the effects of autonomic nerves to involun-
tary muscle and gland cells. On the other hand, the transmission of the
excitatory process across ganglionic synapses, or at voluntary motor nerve

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endings, had the appearance of a direct, unbroken, physical propagation. A single impulse, in a preganglionic or motor nerve, gave rise to, and appeared to be continuous with, a single postganglionic nerve impulse, or a single wave of excitation along the voluntary muscle.   In both cases the transmission delay at the synapse amounted to, at most, a very few milliseconds.   There could be no question, in either of these cases, of a chemical transmitter reaching the ganglion cell or the muscle end-plate by slow diffusion, and normally lingering there in contact with it.   If acetylcholine were to intervene at all in the transmission of these rapid and individual excitatory events, it could only do so by appearing with a flash-like suddenness, as the nerve impulse reached the preganglionic or motor ending.   We must suppose that this abrupt rise of its concentration, taking place in actual contact with the sensitive structures, would excite the ganglion cell to the output of a single secondary impulse along its post-ganglionic axon, or start a single wave of excitation, from the motor end-plate, along the muscle fibre.   And we must further suppose that the acetylcholine, having thus excited this single excitation wave, would vanish almost as quickly as it appeared, within the brief interval of the refractory period, so that, at the end of it, the ganglion cell or muscle fibre would be at rest and fully responsive to the release of another small charge of acetylcholine, by the arrival of another impulse at the preganglionic or motor nerve ending.

When the required conditions are thus considered in detail, it might well seem that such a mode of transmission could be entertained, indeed, as an interesting speculation, but could never be put to the test of practical experiment.   It would seem that the removal of acetylcholine at the required speed could only be effected by its destruction, or fixation, at the site of its liberation.   Evidence of its momentary appearance would, accordingly, be unobtainable, unless this process of its destructive removal could be artificially inhibited.   Here, however, was at least a possibility to be tested; for the only mechanism which could be conceived, in terms of known agents, powerful enough to destroy the acetylcholine with the required rapidity, was a concentration, on surfaces at the nerve endings, of the specific cholinesterase, which destroys it with great rapidity even when in dilute solution; and the action of this might at least be retarded by the use of eserine.   The conception of such a mechanism appeared, in any case, to be highly speculative, and there seemed to be little likelihood that it could be demonstrated experimentally, even if it existed.

It was in the case of the ganglion that we were first emboldened to seek for direct evidence.   Chang and Gaddum (1933), working in my labora-tory, had confirmed an earlier observation of Witanowski, that sympa-thetic ganglia yield acetylcholine to artificial extraction; and they had found that the quantity obtained was proportionately large—larger, indeed, than from any other tissue examined, with the exception of the

quite anomalous cases of the spleens of horses and oxen and the human placenta. Then Feldberg, Minz and Tsudzimura (1934) had observed that stimulation of the splanchnic nerve caused the appearance of acetylcholine in the blood of the suprarenal vein, if eserine was present to prevent its destruction. It appeared to be liberated at the endings of the splanchnic nerve fibres in the medulla, and there to act as the direct stimulus to the output of epinephrine from the medullary cells. Injection of acetylcholine into the arterial blood supply of the gland caused secretion of epinephrine, and Feldberg, who had then come to my laboratory, found that this effect belonged to the 'nicotine' aspect of the actions of acetylcholine. Now the cells of the suprarenal medulla are morphologically equivalent to sympathetic ganglion cells, and the splanchnic fibres which innervate them appear, in the main at least, to be preganglionic fibres. We were evidently getting very near, by analogy, to transmission at the synapses of a sympathetic ganglion; and Kibjakow (1933) had then recently described a method of perfusing such a ganglion. Kibjakow himself, perfusing the ganglion with plain Locke's solution, had, indeed, examined the effect of preganglionic stimulation on the fluid dripping slowly from a cannula in the ganglionic vein. He found that such stimulation caused something to appear in this effluent which, on injection into the arterial side of the perfusion of another, or even of the same ganglion, increased the response of the ganglion to a further period of preganglionic stimulation, or even acted as a direct stimulus to the output of postganglionic impulses; both these effects being observed by recording the retraction of the nictitating membrane. The nature of this substance, which Kibjakow obtained from the stimulated ganglion, has remained a mystery to my colleagues and myself. They never observed the output of any trace of a substance with these stimulating properties, in response to preganglionic stimulation, when the ganglion was perfused with pure Locke's solution. As soon, however, as eserine was added to the perfusion, even in a very low dilution, such as two to five parts in one million, Feldberg and Gaddum (1934) found that stimulation of the preganglionic nerve caused acetylcholine to appear, with perfect regularity, in the venous fluid. The evidence for its identity was of the usual kind—sensitiveness to alkali, potentiation of its effect by eserine, and equivalence to the same known concentration of acetylcholine in a number of different physiological tests. There was no difficulty in carrying out such tests; for, though the fluid could be collected only slowly, it was often so rich in acetylcholine that it required dilution for testing. In no other instance, I believe, has acetylcholine, naturally released by nerve impulses, been obtained in such high concentrations, rising on occasion to one part in ten millions. Such an effluent, reinjected into the arterial side of the perfusion, was capable of producing an outburst of impulses from the ganglion cells. Since it was present in these high proportions, after dilution with

the venous fluid from the whole of the ganglionic tissues, acetylcholine must appear in a much higher concentration at the sites of its liberation; and if these, as seemed probable, were the synaptic endings of the pre- ganglionic fibres, such a sudden appearance of acetylcholine there must act as a stimulus to the ganglion cells. So we argued; and Feldberg and Vartiainen (1934) were able to produce evidence that the acetylcholine was, in fact, liberated at the synapses. They sent impulses, antidromi- cally, back into the ganglion cells by stimulating the postganglionic nerves; and it is well known that impulses in this direction stop short at the cells, and do not cross the synapses. They also stimulated the central end of the vagus, thus sending impulses, without synaptic interruption, through the ganglion of the vagus trunk, which is, of necessity, included in the perfusion with the superior cervical ganglion. In neither of these cases did a trace of acetylcholine appear in the venous effluent during the stimu- lation; it only appeared, and then with great regularity and in compara- tively high concentration, when the preganglionic nerve was stimulated, and the excitatory process passed the synapses. Barsoum, Gaddum and Khayyal (1934) had found that a similar output of acetylcholine occurred from the perfused inferior mesenteric ganglion, when its preganglionic rami were stimulated.

Feldberg and Vartiainen found that, with slow, rhythmical stimulation of the preganglionic nerve, the output of acetylcholine was proportionate to the number of stimuli. From such data, and the known numbers of nerve cells in the ganglion, they could calculate that the arrival of an impulse at a preganglionic ending on one ganglion cell caused the liberation of a quantity of acetylcholine of the order of 10^{-15} gramme. They made the further, highly significant discovery, that the ganglion cells could be paralysed by nicotine, or excess of eserine, so that they were quite unresponsive to preganglionic impulses or to injection of acetylcho- line; but that, under such conditions, stimulation of the preganglionic nerve still caused the output of acetylcholine as usual. There is an obvious and close analogy to the mode of action of atropine on the heart and vagus, as discovered by Loewi and Navratil (1924). More recently Brown and Feldberg (1936) found that an appropriate dose of curarine would paralyse completely the response of the ganglion cells to pregangli- onic impulses or to acetylcholine, and yet leave them normally responsive to the non-specific stimulating action of a sudden rise in the concentration of potassium ions.

The exceptional facilities which the ganglion afforded, for a closely restricted and long-continued perfusion, gave the opportunity of obtaining data concerning the manner of the liberation of acetylcholine by nerve impulses, which probably have a more general application. Observations by Witanowski (1925) and by Engelhart (1930) on the frog's heart, had suggested that each impulse arriving at the vagus endings caused an

immediate, new production, or synthesis, of acetylcholine, so that a period of vagus stimulation might cause it to accumulate in greatly abnormal amount in the heart tissue. Vartiainen (1934), in my laboratory, was unable to repeat these observations, and the evidence seems, on the whole, to be unfavourable to the supposition that each impulse, as it reaches a nerve ending, causes the production by synthesis of the acetylcholine required to transmit its effect. In every tissue which has a cholinergic innervation there is to be found a store, from which acetylcholine can be obtained by extraction. Engelhart (1931) showed in the case of the cat's iris and ciliary body, and Brown and Feldberg (1936, b.) in that of the sympathetic ganglion, that this depôt disappears with degeneration of the cholinergic fibres; so that we may reasonably suppose that it is a part of the ending of a cholinergic nerve fibre, whether postganglionic or preganglionic. It seems probable, therefore, that the arrival of a nerve impulse at the ending causes the liberation from this depôt of a small charge of free acetylcholine. Brown and Feldberg (1936, b.) have further indicated a possible mechanism for this effect. They found that injection of potassium ions into the ganglion caused the discharge of acetylcholine, and its appearance in the venous effluent, just as if the preganglionic fibres had been stimulated. Since there is evidence associating the passage of an impulse along a nerve fibre with the mobilization of potassium ions, it is tempting to think in these terms of the release of acetylcholine from its depôt at the nerve ending. We might picture the impulse, with its wave of mobilization and refixation of potassium, as reaching the ending of the preganglionic fibre, where the momentary appearance of free potassium ions would cause the release of a small charge of acetylcholine; this would act as the immediate stimulus to the discharge from the ganglion cell of a secondary, similar impulse, propagated along the postganglionic fibre, again as a wave of ionic mobilization, until it reached the postganglionic nerve-ending, and there released another specific chemical transmitter of excitation.

Preganglionic stimulation, in any case, causes the liberation of acetylcholine at the synapses, and its appearance in the venous effluent, at such a rate that the whole quantity present in the resting ganglion would soon be exhausted; nevertheless, Brown and Feldberg found that acetylcholine continued to be liberated, at a rate which sank rapidly to a much lower level, but then remained steady as long as stimulation was continued, the impulses being all the time satisfactorily transmitted. In the end, after an hour's continuous stimulation, several times as much acetylcholine had been collected as could be extracted from the resting ganglion, and the amount finally obtainable from the stimulated ganglion was not sensibly diminished. While, therefore, there is no adequate reason for supposing that each impulse produces, by new synthesis, the acetylcholine required to transmit its particular effect, there can be no doubt that, with continued

stimulation, the depôt in the ganglion is replenished by a synthetic pro-
duction which eventually keeps pace with the demand, and enables the
transmission in the ganglion to continue indefinitely, without fatigue due
to exhaustion of the supply.

So far, then, there is abundant evidence for the liberation of acetyl-
choline at the synaptic endings of preganglionic fibres, in a manner and in
amounts adequate to enable it to stimulate the ganglion cells.   We men-
tioned, however, another condition required for its function as the normal
transmitter of excitation at the ganglionic synapses, namely that it must
vanish within the limits of the refractory period which follows the dis-
charge of the first impulse from the ganglion cell, so that a single pre-
ganglionic impulse will evoke a single postganglionic impulse, and no more.
When acetylcholine is applied by injection into the blood vessels of the
ganglion, so that it reaches the ganglion cells by relatively slow diffusion
from the blood vessels, it undoubtedly evokes a repetitive response from
each ganglion cell, with the result that a large and fairly extended response
is obtained from the peripheral effector organ.   In the absence of eserine,
on the other hand, the acetylcholine liberated by preganglionic stimulation
is certainly destroyed with great rapidity, for not a trace of it reaches the
venous fluid.   This is in favour of a local concentration of cholinesterase at
the preganglionic endings; and direct evidence of such concentration has
recently been obtained in my laboratory by v. Brücke (1937), who found
that the sympathetic ganglion normally yields proportionately much
more cholinesterase than the sensory vagus ganglion, used as a control,
but that this excess disappears when the preganglionic nerve degenerates.
Under such conditions, it might be expected that eserine, by delaying the
disappearance from the synapse of the acetylcholine liberated by a single
impulse, would enable it to effect a repetitive stimulation of the ganglion
cell, as when acetylcholine is artificially applied, so that a single pre-
ganglionic would be followed by more than one postganglionic impulse.
The failure to find evidence, that eserine causes such a repetitive trans-
mission, has been used by Eccles as the central point of his argument,
against the function of acetylcholine as the transmitter at ganglionic
synapses.   A little further examination of this argument raises doubts as
to its cogency.   The situation is complicated by the facts that eserine
itself, as we have seen, in more than a very low concentration, has a para-
lysing action on ganglion cells, and that the persistence of acetylcholine in
contact with the ganglion cells, at more than a very low concentration,
has also a secondary, depressant effect.   The complexity of the conditions
thus produced is well illustrated by Brown and Feldberg's (1936, c.)
observations, that, in the course of a continued, rhythmic stimulation of
the preganglionic nerve, with eserine in the fluid perfusing the ganglion,
acetylcholine is liberated in the earlier stages in quantities much in excess
of those required for effective stimulation of the ganglion cells, and its

temporary accumulation has a depressant effect, which is then accentuated either by artificially injecting a small dose of acetylcholine into the perfusion, or by a sudden increase in the strength of the not quite maximal shocks to the preganglionic nerve. Later, the rate of liberation of acetylcholine falls, the excess is washed away, and the depression with it; and now a similar, temporary increase in the strength of the shocks to the preganglionic nerve, or an injection of acetylcholine, has a purely potentiating effect on the discharge from the ganglion cells, as revealed by the response of the effector organ. We are certainly not in a position, as yet, to give a full and detailed explanation of such complexities and apparent anomalies; we cannot yet define the conditions under which continued access of acetylcholine to a ganglion cell may produce, on the one hand, a repetitive discharge of impulses, and, on the other, depression of the responsiveness of the cells. Meanwhile, it hardly seems justifiable to regard the failure of eserine, to produce a repetitive discharge which the electrical record can detect, as sufficient, by itself, to exclude the action of acetylcholine as transmitter at the ganglionic synapses, in the face of such a concordance of directly favourable evidence of other kinds.

It required success with the ganglion to embolden us to tackle the case of the voluntary muscle. There was a tremendous body of tradition, in favour of a physical propagation of the excitatory wave from motor nerve ending to voluntary muscle fibre; and, if a chemical transmitter were supposed, by analogy, to intervene at this point, its demonstration would present additional difficulties of a quantitative nature. For if, on the analogy of the ganglion, acetylcholine were concerned with the transmission of excitation from motor nerve to voluntary muscle, it should be liberated only at the endings of the motor nerve fibres on the motor endplates. And, whereas the small ganglion is closely packed with synapses, so that acetylcholine appears in relatively high concentration in the slowly percolating perfusion fluid, there is only one motor nerve ending to each of the fibres composing a large muscle, and only a very small proportion, of the large volume of fluid perfusing such a muscle, would pass even in the neighbourhood of these scattered nerve endings. Even if acetylcholine were liberated at these motor nerve endings by the arrival of impulses, we could only expect it, accordingly, to appear in a very low concentration in the fluid flowing from the muscular vein. We shall see that this expectation was realized. Before mentioning our own experiments, however, I ought to draw your attention to the fact that several earlier observers had obtained evidence of the liberation from perfused frog's voluntary muscles, when these were stimulated through their nerves, of something acting like acetylcholine (Hess, 1923; Brinkman and Ruiter, 1924, 1925; Shimidzu, 1926). In all cases, however, they had stimulated the mixed nerve, and even the authors themselves did not definitely associate the effect with the motor fibres, or with the transmission of excitation

to the voluntary muscle fibres. My colleagues and I made most of our experiments on mammalian muscles, and success was only obtained when these were perfused with warm Locke's solution, containing a low concentration of eserine. This complicated the experiments and limited their scope; for the mammalian muscle, when so perfused, early begins to become oedematous, and the experiment has then to be terminated. Nevertheless we succeeded in proving that, when such a muscle is effectively stimulated through its motor nerve fibres alone, the autonomic and sensory components of the ordinary, mixed muscular nerve being excluded, a substance having the properties of acetylcholine regularly appears, in low concentration, in the venous effluent, and disappears again when the stimulation is stopped (Dale, Feldberg, Vogt, 1936). It is a substance sensitive to esterase and to an alkaline reaction, equivalent in action to the same dose of acetylcholine in a series of different biological reactions. There can be no doubt that it is acetylcholine. I said that the concentration was low; but we have seen reasons for expecting that it would be so. And when, from the total quantity liberated by a known number of shocks, and the number of fibres in the muscle, we attempted to calculate the quantity liberated by one impulse, arriving at one motor nerve ending on a motor end-plate, we obtained a quantity of the same order as that which we had previously calculated for the ganglion cell, namely, 10^{-15} gramme.

We regularly observed this output of acetylcholine from the muscle when its motor nerve supply was stimulated, or when the shocks were sent directly through the normal muscle, with intact nerve endings. If the nerve was caused to degenerate, however, stimulation of the denervated muscle, though it contracted vigorously, produced no trace of acetylcholine. On the other hand, if the normally innervated muscle was rendered completely unresponsive to nerve stimulation, by adding curarine to the perfusion fluid, stimulation of the motor nerve caused the usual output of acetylcholine, from a completely passive muscle. The appearance of acetylcholine was clearly associated with the neuromuscular transmission, and not with the mechanical response; and the effect of curarine here, like that of nicotine or curarine on the ganglion cells, was again closely analogous to that of atropine on the heart.

In the case of the voluntary muscle, however, the suggestion that acetylcholine acted as the transmitter of excitation, from the motor nerve ending, had additional difficulties to meet. Certain voluntary muscles, indeed, as I had noted already in 1914, were known to be stimulated by acetylcholine, as by other choline esters. But the reactions of these muscles to acetylcholine, whether they were normal muscles of frogs (Riesser and Neuschloss, 1921), or birds (Gasser and Dale, 1926), or the denervated muscles of mammals. (Frank, Nothmann and Hirsch-Kauffmann, 1922; Dale and Gasser, 1926), appeared to be slow contractures, having no certain relation to the stimulation of a voluntary muscle to its

characteristically quick, propagated contraction. As for the normal muscles of mammals, they had been seen to give contractions of a quicker type in response to injections of acetylcholine (Feldberg, 1933; Feldberg and Minz, 1931; Simonart and Simonart, 1935 a & b.); but these were, at best, inconstant in appearance, and normally required large dosages for their production. It appeared to my colleagues and myself, however, that the application of acetylcholine by ordinary methods, whether it was applied in a bath to the surface of a muscle, or injected into the general circulation, could not reproduce anything like the sudden rise of its concentration which would be produced at the motor end-plates of the muscle fibres, if it were indeed liberated there by the arrival of impulses at the contiguous motor nerve endings. A motor nerve volley, caused by a maximal shock applied to the nerve, would cause this abrupt appearance of acetylcholine simultaneously, at every motor end plate in the muscle; and it was not to be expected that the resulting twitch could be imitated by allowing acetylcholine to soak into the muscle from its surface, or to be carried to it by the general circulation. We could not expect, indeed, by any means of artificial application of acetylcholine, to reproduce the suddenness and the simultaneity of its access to all the motor end plates, if it were released at the nerve endings by a motor nerve volley. But we could endeavour to make a nearer approach to this speed of access, by rapidly injecting a small dose of acetylcholine, in a small volume of fluid, directly into the blood vessels of a muscle, when the blood had been allowed to drain out of them after brief clamping of the main artery. We tried this method, and with doses of two to five γ only of acetylcholine, in 0.25 to 0.5 cc., thus suddenly injected into the empty blood vessels of a cat's gastrocnemius, we obtained quick contractions, which superficially resembled rather slow, single twitches. (Brown, Dale & Feldberg, 1936.) Even two γ would, in a favourable preparation, produce a contraction of as high a tension as a maximal motor nerve twitch, and taking only about twice as long to reach that tension; while twenty γ would produce a quick contraction to three or four times the maximal twitch tension. Of course, only a small part of the dose so injected would reach the end plates of the muscle fibres; and it would not vanish suddenly after starting a single excitatory wave along each muscle fibre, but would be kept at a stimulating concentration, possibly through several refractory periods, by diffusion from the tissue spaces of the muscle. We should therefore expect the contractions produced by the quickest possible injections of acetylcholine into the blood vessels of the muscle, to be short bursts of asynchronous tetanus; and the electrical records, taken by my colleague, G. L. Brown (1937), showed that they had that character. They were not contractures; they were produced by summation of the asynchronous, repetitive, propagated twitches of the individual fibres. They were, in fact, exactly the kind of responses that a chemical transmitter of motor

nerve excitation might be expected to evoke, if it were thus applied by artificial injection. It was further in accordance with the conception of acetylcholine as the neuromuscular transmitter, that these quick reactions to it of normal mammalian muscle were readily suppressed by curare; acetylcholine contractions, of the same tension as maximal nerve twitches, disappeared rather earlier than the latter under curarization.

The difficulty due to the supposed insensitiveness of normal mammalian muscle seemed thus to have disappeared. If acetylcholine, however, were to be regarded as the transmitter of motor nerve excitation, we could not limit its function to the mammal, and the frog's muscle, which had been found to respond to acetylcholine by a slow contracture of low tension, relatively resistant to curare, presented the next problem. Here again, rapid injection of small doses directly into the muscular artery, carried out by G. L. Brown (1937b.), has produced a remarkably different type of response. If 1 γ of acetylcholine, in 0.1 c.c. of Ringer's solution, is thus injected into the vessels of a normal frog's gastrocnemius, a very striking and immediate response is observed. The whole surface of the muscle, covered by a glistening aponeurosis, ripples and quivers with the asynchronous contractions propagated along its constituent fibres. A mechanical record shows the development of a tension of two hundred grammes or more at the height of this irregular tetanus; and an electrical record shows a long outburst of quick changes of potential. With larger doses there is an initial outburst of tetanus, cut short, however, by the onset of a secondary contracture, with which the electrical disturbances are completely silenced. A very similar sequence of effects is seen, with an even lower scale of dosage, when acetylcholine is administered by close arterial injection to a denervated mammalian muscle (Brown, 1937, b.). The frog's muscle also, when denervated, shows the same sequence of pure tetanic response with the smallest dose, and tetanus cut short by contracture with a higher dose, the series of doses for production of these effects being on a reduced scale. The results strongly suggest that the normal frog's muscle, in its responses to acetylcholine, is, in some sense, intermediate between the normal and the denervated mammalian muscle, though nearer to the latter, as witness the relatively small and almost purely quantitative change in the reactions of the frog's muscle when it is denervated.

In conjunction with direct evidence obtained on the ganglion, these facts strongly suggest that the effects of denervation on the response of the voluntary muscle to acetylcholine are due, in part, to a disappearance, from the neighbourhood of the nerve ending and the muscle end plate, of a normal concentration of cholinesterase, though the sensitization cannot be entirely due to this, since it also affects the reactions to such substances as nicotine and tetramethylammonium salts, on which cholinesterase has no action. Incidentally the evidence suggests that this local concentration of

cholinesterase is less effective in the normal frog's muscle than in that of the
mammal. We thus come naturally to the question of the other condition
requisite for the action of acetylcholine as the transmitter of excitation
from motor nerve to voluntary muscle, namely its immediate removal
after it has started a single wave of excitation from the muscle end plate.
As in the case of the ganglion, we enquire whether eserine, by depressing
the cholinesterase action, will delay this disappearance of acetylcholine,
and thus produce a repetitive response of the muscle to a single nerve
volley. The picture in this case is not complicated by a paralysing action
of eserine, and its effect is clear and unmistakable (Brown, Dale and
Feldberg, 1936). It converts the response which the muscle gives to a
single, maximal nerve volley, normally a single twitch, into a short burst
of tetanus, fading out rather than terminating abruptly, and producing
a maximum tension which may be as much as five times that of the single
twitch. Brown's electrical records showed clearly the nature of the
response, as a short, waning tetanus, and Bacq and Brown (1937) have
examined a series of eserine substitutes, and found that they produce
this potentiating action, on the muscular response to a single nerve volley,
in direct proportion to their depressant actions on cholinesterase, as
independently determined.

There is another aspect of the action of eserine, however, which must be
mentioned. Other observers, such as Rosenblueth, Lindsley and Morison
(1936), found that the response of the mammalian muscle to single, max-
imal nerve volleys was depressed, rather than enhanced, by eserine. The
reason of this apparent discrepancy has been discovered, independently,
by my own colleagues (Bacq and Brown) and by Rosenblueth and his
co-workers. If the volleys follow too quickly after one another, the
potentiation is completely obscured by a secondary depression, which
can only be attributed to accumulation of acetylcholine because each
impulse releases a further quantity, before more than a part of that due
to the foregoing impulse has disappeared. Bacq and Brown have
shown, indeed, that, under such conditions, a short burst of tetanization
through the nerve will cause a subsequent depression of the response
to single nerve volleys, which can be very closely reproduced by a small
injection of acetylcholine into the blood vessels of the muscle. Here,
then, we meet again the secondary, depressant action, due to persistence
of acetylcholine at the point of its action. We have seen how it compli-
cates the response of the ganglion cells to preganglionic impulses in the
presence of eserine, and it undoubtedly accounts for some of the differ-
ences observed between the frog's muscle and that of a mammal, as re-
gards the effect of eserine on its response to maximal nerve volleys. A
few weeks ago, I should have stated that the potentiating effect of eserine
on the response of amphibian muscle to nerve volleys had not yet been
demonstrated; but, even as I write, I receive from Dr. T. P. Feng, of

Peiping, an advance copy of a paper he has in the press, which shows that a toad's muscle gives the same potentiated responses after eserine as a mammal's, if the nerve volleys are separated by intervals, not of ten seconds, but of five minutes.

So far has investigation led us. There is clearly an urgent need for more. Many points still remain obscure, and many difficulties are yet unresolved. Yet the evidence already before us seems to me to point clearly to a conclusion. I think that we must be prepared to consider an extension of the transmission of excitation by the liberation of acetylcholine, now long familiar for peripheral autonomic effects, to all the synaptic and neuromuscular junctions of the peripheral nervous system, whether voluntary or autonomic, with the exception of the peripheral sympathetic fibres, which similarly employ an epinephrine-like substance, or 'sympathin'. I have on an earlier occasion (Dale, 1935), drawn attention to the conformity between this classification and Langley and Anderson's experiments on crossed regeneration. Their results, I suggested, could be summarized in the statement that only fibres which act by liberation of the same chemical transmitter can functionally replace one another. At the time there was no clear evidence that the sensory fibres might also be cholinergic, and Langley and Anderson's (1904) results seemed to indicate otherwise. Since then, however, P. Weiss (1934) has shown that either the central or the peripheral ends of sensory fibres, in the toad, can be made functionally to replace the motor fibres to a voluntary muscle; and Wybauw (1936) has obtained direct evidence that the antidromic, vasodilator branches from sensory fibres are cholinergic. There is, on the other hand, evidence from several sources of a relatively high acetylcholine content in certain parts of the brain, and, recently, the highly suggestive demonstration, by the Stedmans (1937), of a synthesis by minced brain tissue, in the presence of eserine and chloroform, of acetylcholine in such quantities that it could be isolated and chemically identified. Whither is such evidence leading us? Will the concept of transmission by liberation of acetylcholine have to be extended even to some central synapses? I cannot answer. I can only plead that an extension of such importance should not be made on a basis merely of suggestive analogy, but only in the light of direct and critically scrutinised evidence.

There remains one other question, on which I ought to touch briefly in conclusion. We have seen that Feldberg and Vartiainen (1934) failed to obtain evidence of the liberation of acetylcholine when they stimulated the vagus nerve, the fibres of which pass through the vagus ganglion without synaptic interruption, or when they stimulated antidromically the postganglionic fibres from the superior cervical ganglion. They concluded that acetylcholine was liberated at the synaptic endings of preganglionic fibres, and not from nerve fibres at other points of their

course. The evidence from work on striated muscle, though the point could not there be made the subject of such direct experiment, pointed in the same direction. In both cases it seemed to correspond to the libera-tion of acetylcholine only at those points where it would immediately make contact with structures demonstrably sensitive to its action, and would thus serve as a physiological transmitter of excitation. The survey made by Chang and Gaddum (1933) led to the conclusion that the distribution of acetylcholine in the body tissues, with certain conspicuous and unexplained exceptions, is on the whole related to this physiological function of transmitting the effects of cholinergic nerve impulses from the nerve endings. The question, however, remained open, whether this difference, between the endings of cholinergic nerve fibres in relation to effector cells or at interneuronal synapses, and the rest of such fibres, was absolute and qualitative, or merely quantitative. Barsoum (1935) found that nerves, and certain autonomic nerves especially, yield rela-tively large proportions of acetylcholine to extraction. There is certainly no evidence that acetylcholine applied artificially to any nerve trunk has a perceptible stimulating, or other physiological action upon it. On the other hand, there is evidence, chiefly from Italian physiologists (Calabro, 1933; Bergami, 1936a and b), that small proportions of a substance behaving like acetylcholine are liberated from a mammalian nerve (vagus, phrenic, etc.), into a Ringer solution into which it is allowed to dip, either when the nerve is stimulated artificially, or even when normal, physiolog-ical impulses pass along it from the nerve centres. The conditions, as regards the composition of the Ringer solution requisite for success, seem to be rather artificial; and it is difficult to picture a function for the release of acetylcholine, as the impulse passes along an intact nerve, which could find a place in any yet extant theory of the nature of the nerve impulse and its propagation. It can only be said at present that the phenomena described have such interest and importance, that it may be hoped and expected that attempts to confirm them and further to explore their significance will be undertaken in other laboratories. If the liberation of a chemical mediator at a nerve ending should prove to be, not a process peculiar and limited to that ending, but merely a local intensification, to ensure transmission to a contiguous cell, of a process which actually figures in the propagation of the impulse along the nerve fibre, we should have to make yet a further revision of our existing conceptions. Some minds have undoubtedly felt difficulty in postulating a complete breach in the nature of the processes concerned in transmission, where the excita-tion passes from nerve ending to effector cell. This particular difficulty would then disappear, but only at the cost of a more fundamental change of conception concerning the nature of the propagated wave of excitation. than any which has yet been seriously considered.

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MOUNT SINAI IN THE LATE NINETIES AND THE BEGINNING OF NEUROSURGERY IN THE HOSPITAL

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During a period of thirty-five years, from 1893 to 1927, the writer was in succession an intern, assistant pathologist and a member of the surgical attending staff. The story that he has been asked to tell does not concern the enormous development of the hospital in the later years of this period, but the conditions which existed in the nineties and the early part of this century. Some of the facts here recorded may be of local historical interest, others may appear amusing, some savor of pathos. One can not write of the Hospital without mention of those who labored in it. Many of the latter are no longer with us, but their influence has remained.

At the present day, it appears natural that female nurses should be in charge of hospital wards both those for women and for men. The existence of the modern hospital without a properly equipped pathological and bacteriological laboratory seems impossible. An operating room without specially trained personnel, special materials and instruments appears a relic of the past. Today nobody will doubt the justification for specialism, for no single individual can encompass the entire field of medicine and surgery.

THE HOSPITAL IN GENERAL

The writer well remembers his days as an intern on the medical and surgical services. There were, of course, male and female wards, but the male wards were supervised entirely by orderlies, and it required many meetings of the Medical Board and the Board of Directors to overcome the supposed impropriety and indelicacy of having women in charge of wards for male patients. From the war in Crimea and Florence Nightingale in 1855 to the Hospital in the nineties seems a long period, but the history of the past shows that the influences of times and customs are slowly overcome. I believe that I am correct in the statement that no one was more influential in bringing about this change than Dr. Gerster, whose force of character, energy and high ideals have had a lasting effect upon surgery at The Mount Sinai Hospital and upon the Hospital organization.

When the writer began his internship at the Hospital, there were general medical and surgical services, and separate wards for gynecology, pediatrics and diseases of the eye. If a child on the pediatric service developed empyema, the operation was performed by the attending staff of the pedi-

atric service and not by the surgeons of the Hospital.   Ophthalmological operations were performed in the eye wards and not in the operating rooms. The separation of otology from ophthalmology had not yet been brought about, and Dr. Gruening had charge of the patients with diseases of the eye, ear, nose and throat.   There were special wards for diseases of the eye, but patients with ear diseases were in the general surgical wards, and laryngology was mainly an out-patient service.   There were no special wards for neurology, orthopedics, otology or laryngology, but there were consultants,—Dr. B. Sachs for neurology, Dr. Frederick Whiting for otology, Dr. S. Lustgarten for dermatology, and later Dr. Emil Mayer for laryngology, and Dr. P. W. Nathan for orthopedics.

In the early nineties, there was, of course, no X-ray department, for it was only in 1895 that Roentgen discovered the ray which bears his name, and several years passed before the practical value of the discovery was fully appreciated.   In Mount Sinai the first X-ray machine was set up in a corner of the synagogue and was used by some of the members of the attending staff on the days when there were not any religious services.

The first attending neurologist to the hospital was Dr. Sachs and the first attending laryngologist, Dr. Emil Mayer.   Later, an orthopedic service was begun under Dr. P. W. Nathan, and a dermatological service under Dr. Hermann Goldenberg.   Dr. Sachs, hale and hearty, is still active in his profession, but the others have passed into the Great Beyond.   Emil Mayer had a lovable personality, and skill and judgment in his special field.   He was succeeded by Sidney Yankauer, whose unusual dexterity for delicate intranasal operations and remarkable mechanical talents were appreciated by all.   If he had chosen engineering instead of medicine, he would have attained an equally eminent position.   Philip W. Nathan brought to the orthopedic service the large experience and skill for which he was so well known.   Hermann Goldenberg, whose death occurred very recently, was admired both for diagnostic acumen in dermatology and for his modest and sincere personality.   I would like to say more of all of these old friends; each has left an indelible impression upon the roster of Mount Sinai Hospital.

THE PATHOLOGICAL LABORATORY

On the second floor of the north wing of the old hospital building on Sixty-seventh Street was the gynecological ward in charge of Dr. Mundé. Through the energy of Dr. H. Newton Heineman, one of the attending physicians, a pathological laboratory was started in 1893.   A small room on the second floor (x on the accompanying photograph) was set apart for this purpose and the laboratory was put in charge of Dr. Mandlebaum. This small room witnessed the birth of pathology and of bacteriology in our institution.   As elegant a technician as he was a fine gentleman, Frederick S. Mandlebaum devoted himself to the new laboratory.   He not

only studied the gross material received from the operating room and from autopsies (which he himself performed), but he did all the cutting and staining of sections, and in addition cleaned and dusted the laboratory room. When the writer became assistant pathologist, one of his duties was to help in keeping the place clean and this included mopping up of the floor. A "diener" for this purpose was supplied only many years later. As chance would have it, the new assistant pathologist started bacteriology in the Hospital. As there was no one to help, we had to clean test tubes, prepare culture media and sterilize and clean the test tubes after they had been used. The one thermostat was heated by a gas-burner and on account of fire danger, the Hospital authorities objected to the

The Mount Sinai Building on 67th Street. x shows the location of the Pathological Laboratory.

burner being on all night without anyone to watch it. So for a time whenever cultures were being grown, we had to stay in the laboratory all night and keep a watchful eye on the thermostat! The laboratory soon became a meeting place for many members of the attending staff, its work rapidly increased, and its influence steadily broadened. This single room was the hospital laboratory up to the time when the new buildings were constructed and occupied. In this room Dr. Mandlebaum carried out the studies which gave him a high reputation as a pathologist, and in the same place the first studies in America of the Widal reaction in typhoid fever were carried out.[1] It was possible to trace an epidemic of typhoid fever

[1] Elsberg, C. A.: The Serum Reaction in Typhoid Fever. New York Medical Record, April 10, 1897.

among the nurses to an employee who was probably a typhoid carrier, and to investigate the Widal test in those who had the disease and those who had been exposed to the infection.

White mice, rabbits and guinea-pigs were kept in a cage in the sub-basement of the Hospital. In the daytime the cage was rolled out into the hospital yard and at night was kept in one of the corridors. If one can apply the term to an animal cage, this cage had a checkered career. One day a grocery wagon upset the cage and the guinea-pigs and mice escaped and frightened convalescent patients who were sitting in the yard. As a result, considerable diplomacy was required before permission could be obtained to continue to keep the animals.

THE OPERATING ROOM AND THE BEGINNING OF NEUROSURGERY IN THE HOSPITAL

Neurology and neuropathology are outgrowths from general medicine and general pathology. The Mount Sinai Hospital was the first general hospital in New York to recognize the importance of diseases of the "master tissue" of the body, by the organization of a service and wards for neurology—which was to no small degree due to Bernard Sachs. Later, due to the energy of the Editor of this Journal, a special laboratory for neuropathology was organized. But in the nineties there were no neurological wards and no laboratory for neuropathology. Patients with diseases of the nervous system were in the general medical wards and the consulting neurologist was called in when necessary. The special silver stains devised by Golgi and Cajal, which have meant so much for the advances in our knowledge of the histology of the nervous system in health and disease, and which have so greatly influenced our understanding of the pathology of tumors derived from glia and from nerve tissue, had recently been devised. What these methods have meant for neuropathology only those can fully appreciate who worked during the period when gliomas were divided into the solid and the soft, and were classified either as gliomas or gliosarcomas. The dawn came when one of our own hospital investigators first recognized the histological entity which he called spongioblastoma multiforme—a name that, in the future, will again come into general use instead of the term now popular, which characterizes a cell type which has no existence in fact.

In order to appreciate the beginning of neurosurgery in The Mount Sinai Hospital, we must turn for a moment to a consideration of the conditions which existed in the operating room in the closing years of the nineteenth century.

The firm belief of Dr. Gerster in antiseptic and aseptic surgery, shown by the publication of a book on this subject,[2] resulted in the application

[2] Gerster, A. G.: The Rules of Aseptic and Antiseptic Surgery. D. Appleton & Co., New York, 1880.

of the newest methods, which for those days were highly efficient. When the writer was an intern on the surgical service, antisepsis in the operating room had been in part replaced by aseptic methods. The carbolic spray had been discarded, but the instruments were still kept in carbolic solution. Dr. Gerster insisted upon the most rigid aseptic and antiseptic technique, and in this respect was far ahead of many surgeons of his day. The full significance of this can be appreciated when, in a book on brain surgery published in 1893,[3] an eminent neurologist found it necessary to make the following serious statement which today seems almost amusing: "It is an absolute requisite of success in cerebral operations that every detail of aseptic surgery should be carried out to perfection. It is useless to make elaborate preparations, to sterilize instruments, and to apply antiseptic solutions to the hands, if in the midst of the operation the surgeon stops for a moment to adjust his septic eyeglass, or to blow his nose on a septic handkerchief without subsequently washing his hands again."

In the Hospital on Sixty-seventh Street, there was only one operating room. As a result a surgically clean operation would often follow immediately upon the opening of an abscess. Thus the writer remembers an occasion when during the course of one strenuous night the following operations were performed in succession: incisions for abscess of the breast, herniotomy for strangulated inguinal hernia, appendectomy and drainage for gangrenous appendicitis with abscess, laparotomy for acute intestinal obstruction. The house surgeon assisted at or performed the operations. This was before the time when there were rubber gloves and therefore wound healing depended upon the scrubbing of the hands of the operating team. In spite of this, most of the sutured wounds healed by primary union.

About the time when cranial operations increased in number, a small room was set aside for so-called "pus cases," and the first step was taken to prevent wound infection in operations upon the brain and spinal cord as well as in other clean wounds.

It is a curious and interesting fact that the surgery of the spinal cord in which the technical problems which have to be met by the surgeon are less, was developed in The Mount Sinai Hospital (and likewise in other institutions) years after the surgery of the brain.

In those days, operations for tumor of the brain were rare, but surgery for epilepsy had been done frequently by Dr. Gerster as shown by papers by Sachs and Gerster published in 1892 and 1896.[4]

Dr. Gerster used the hand trephine to make the first opening in the skull and at first removed the bone with rongeurs as was done by Victor Horsley.

[3] Starr, M. Allen: Brain Surgery, New York, 1893.
[4] Sachs, B. and A. G. Gerster: Trephining for Epilepsy. Am. J. Med. Sci., November, 1892; The Surgical Treatment of Focal Epilepsy, Am. J. Med. Sci., October, 1896.

Later he made the osteoplastic bone flaps first devised by Wagner in 1889, and used an electrically driven saw. Due to the rigid aseptic precautions he insisted upon, and to his technical skill, the results of his cranial operations were remarkably good for those days. Modern cranial surgery had, however, not yet been born, and the hospital records of the time show that during the course of each year few operations for tumor of the brain were performed.[5]

This was due to the limited knowledge regarding tumors of the brain, to the difficulties of diagnosis and localization, to the still undeveloped technique and to the fact that diagnosis and localization were considered to be "purely medical questions and until they are decided the surgeon can not be asked to operate." In other words, the surgeon was merely the technician, who was expected to operate in the area pointed out to him by the neurologist. Neurological surgery was just a part of general surgery!

Soon, however, it became clear that the surgery of the nervous system could be developed only if neurosurgery was split off from general surgery, and the neurosurgeon was given the opportunity to develop the technique and to gain an adequate knowledge of neurology. For operations upon the brain and spinal cord can only be properly performed by the neurological surgeon if he has a precise knowledge of the diagnosis and localization of diseases of the brain and spinal cord. No doubt the papers published by Harvey Cushing[6] did much to popularize this viewpoint and they had their influence in The Mount Sinai Hospital.

As a result, patients who required operations on the brain or spinal cord were at first transferred to one surgical service (that of Dr. Lilienthal) and soon thereafter the operations were performed by one of the surgeons on that service—the writer.

In the opening years of this century, the development of the special field of neurological surgery was greatly aided by the improvements in diagnosis and localization brought about the method of encephalography and ventriculography which followed the discovery of the Roentgen rays and the methods of X-ray examination of the skull and spine. That air in the ventricular cavities is visible on X-ray films of the skull was due to the observations of a former house surgeon of The Mount Sinai Hospital, William H. Luckett, who was the first to report the finding of air in the ventricles on X-ray plates of a patient with a fracture of the skull.[7] This led to the procedure of injection of air by Dr. Walter E. Dandy.

When the medical and lay boards of the hospital adopted the broad-

[5] Stieglitz, L., Lilienthal, H. and A. G. Gerster: A Study of Three Cases of Tumor of the Brain. Am. J. Med. Sci., March, 1896.

[6] Cushing, Harvey: The Special Field of Neurological Surgery. Bull. Johns Hopkins Hospital, 16:77, 1905.

[7] Luckett, W. H.: Air in the Ventricles following a Fracture of the Skull. Surg., Gynec. & Obst., 17: 237, 1913.

minded and progressive view of the justification for specialties in surgery, and particularly of the specialty of neurological surgery, the stage was set for the further development of this special field. Difficulties arose however, which required years of effort and propaganda before they could be overcome. The hospital authorities could not understand that the technique of neurological surgery required a special trained personnel and special materials. More than one year elapsed before the writer could obtain the gray materials for towels and for sheets which are so important to prevent visual fatigue in the often greatly prolonged cranial operations. Likewise a period passed before the authorities were convinced of the justice of the demand that an operating room nurse, to be able to assist at operations upon the central nervous system should have had special training in the methods used in those surgical procedures and the special materials and instruments that are required. And the request that a special operating room be set aside for operations upon the central nervous system and that a special neurosurgical service should be created, was, at that time, considered central and not stereoscopic vision of the field of neurological surgery in its relation to general surgery! However, in spite of the difficulties that had to be overcome, all of this has been finally brought about, and today in The Mount Sinai Hospital, neurosurgery is a specialized field which has an intimate affiliation with neurology and with neuropathology. Each has its own organization, but the working together is due to the synaptic relations between them. The advantages of this arrangement are evident now and will be more strikingly appreciated as time goes on.

DIETARY SUGGESTIONS FOR THE MANAGEMENT OF DIABETIC PATIENTS USING PROTAMINE ZINC INSULIN

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The use of insulin retard requires a diet whose carbohydrate availability is retard. With the introduction of protamine insulin, it became apparent that the standard diets, as used with the old insulin, were not suitable. It stands to reason, that with the quick acting insulin, the speed of availability of carbohydrate could be quite variable. With the average latent period of the old insulin varying from fifteen minutes to one hour and the maximum duration of action four to six hours, one was not concerned with prolonging or delaying the carbohydrate availability. With protamine insulin the problem is quite different. This slow acting insulin begins to exert its maximum activity after a latent period of approximately three hours. This action can be prolonged, depending upon the carbohydrate to insulin ratios, from twenty-four to forty-eight hours, that is in the fasting individual, for Wilder and his co-workers have shown that evidence of activity of the insulin is still present after more than thirty-six hours. It becomes important then to try to make the period of maximum activity and duration of the protamine insulin coincide with the period of maximum availability and the duration of availability of the carbohydrate.

The use of the old standard diets with protamine insulin very frequently gave rise to post-breakfast glycosurias, as well as frequent pre-breakfast hypoglycemic manifestations. Attempts to increase the amount of insulin to control the post-breakfast glycosuria, resulted in more severe hypoglycemia the following day. This has led to the device of multiple injections, i.e. supplementing the protamine insulin with a small dose of regular insulin before breakfast, to control the immediate post-breakfast glycosuria. However, this device did not solve the next morning's hypoglycemic period. It was found that when one decreases the amount of protamine insulin to prevent the early morning hypoglycemia, it is not uncommon to have the patient develop glycosuria in the evening period, which then requires another injection of regular insulin, thus resulting in three injections of insulin daily. This is an unnecessarily complicated procedure and depreciated one of the virtues of protamine insulin, the sufficiency of only one daily injection.

From clinical observations and from experimental data, it became quite evident that certain of these problems could be solved by shifting the diets to conform with the individual patients' particular reactions. It has been known for a long time that when glucose entered the blood stream above certain critical rates even in normal people, glycosuria resulted; that if this administration was continued the glycosuria and hyperglycemia decreased and even disappeared. The routine glucose tolerance test as practiced daily reveals this same tendency, i.e. an initial rise in the first hour with the subsequent drop, frequently falling below the fasting level. It is this rapid elevation of blood sugar after glucose ingestion which produces the post-breakfast glycosuria in the patient using protamine insulin. It is logical to assume, if the availability of the ingested carbohydrate could be retarded, that the glucose would enter the blood stream at a rate slow enough to be disposed of and the temporary glycosuria and hyperglycemia eliminated. From evidence obtained and soon to be published, it is apparent that the avoidance of the hyperglycemia would result in the avoidance of the hypoglycemia in the majority of cases. It is not uncommon to find that those patients who complain of hypoglycemic reactions in the middle of the day, as differentiated from such who have hypoglycemia in the early morning, are those who have the post-prandial glycosurias.

An analysis of the diets of the majority of our diabetic patients revealed that the standard breakfast called for one portion of twelve per cent fruit usually consumed as fruit juice. Fruit juices for practical purposes represent glucose solutions, readily absorbed and digested. This was recognized for years, as observed in the prompt response of insulin shock, to orange juice by mouth. Thus it should not be surprising to find that patients using protamine insulin and drinking fruit juice should frequently have post-breakfast glycosuria. Furthermore, it must be remembered that the breakfast carbohydrate is being taken care of by the protamine insulin administered on the previous day, and has spent almost all of its activity; also, that the protamine taken in the morning begins first to do its work at the lunch period. This leads to the recognition of two definite principles with regard to the breakfast of the patient using protamine insulin:

One: the avoidance of fruit juices and most fruits.

Two: the use of small breakfasts.

As to the fruits, work is now being carried on by Dr. Dolger and myself, on the relative *rates of availability* of all fruits, as well as those of other common forms of carbohydrates. This much can be said now: there is a difference in the rate of availability of the carbohydrates in various fruits.

The problem of avoiding the midnight and early morning hypoglycemia

resolves itself into one of trying to provide a constant supply of carbohydrate to the body throughout the night. Attempts to satisfy this demand have led to the practice of small midnight meals of milk and crackers etc., but this is not always satisfactory.

It is known that about fifty per cent of the protein ingested is available to the body as carbohydrate. It is also well known that the emptying time of the stomach after a meat meal may be as long as three hours. Hence, in order for this protein to become available to the body as glucose, it must then be completely digested, the amino acids carried to the liver, deaminated and the residual molecular fragments re-synthesized into glucose, processes which take considerable time.

Conn and Newburgh, in their publication in the Journal of Clinical Investigation on the use of high protein diets for the treatment of spontaneous hypoglycemia, have given added proof to the related theoretical concepts. Their curves showing the prolonged availability of the carbohydrate fraction of protein, seemed to give the desired answer in our problem. Accordingly, we introduced a third change in our standard diets. It resulted in feeding of a large portion of protein food at the evening meal and advancing the evening meal as late as possible, (most people object to taking dinner routinely after 7 to 7:30 P.M.). Occasionally it even becomes necessary to have the patient take a portion of meat at bed-time. Most of them avail themselves of the opportunity of eating a "Hamburger steak" at night. This change in diet plan has resulted in raising the level of the pre-breakfast blood sugars from an average of 70 to 100 in the well controlled patient.

In accordance with these observations, it is now our custom to prescribe for all patients the following initial routine:

a) Diets limited to a maximum of 150 g. carbohydrate at the start. Higher carbohydrate diets make the control more difficult and, at times, impossible with protamine insulin. The carbohydrate may be raised later, after full control has been established.

b) Carbohydrates divided into 1/5, 2/5, 2/5 for breakfast, lunch and supper respectively.

c) The use of all fruits and fruit juices for breakfast, with but few exceptions, is prohibited.

d) Proteins are divided into 1/6, 1/6, 2/3 for breakfast, lunch and supper respectively.

e) Protamine insulin is used once daily before breakfast.

In view of the principles of delayed emptying time of the stomach, further studies are in progress on the addition of fats at breakfast, such as heavy cream in various cereals and in fruits. The use of bacon and eggs at night time has shown that this addition of fat prolongs the duration of the carbohydrate availability of the protein.

It must be stated clearly that this is only a basis for initiating a control of the diabetic status. All patients will not yield to control by this procedure, but the majority of them will respond well and be controlled with greater ease on such a regime. The latter has as its advantage the simplicity of a single injection of insulin daily. Indeed, there is a small group of patients whose control cannot be achieved by the above routine and require supplementary doses of regular insulin. Nevertheless, the regime outlined above facilitates the approach to the control of diabetes in an appreciably large number of patients.

COMPLETE CHANGE OF VENTRICULAR PREPONDERANCE IN THE ELECTROCARDIOGRAM

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Marked change in ventricular preponderance is not a common event in the course of valvular heart disease. When such a change does occur, it usually indicates anatomical changes, and the electrocardiogram may then assume diagnostic importance. This is illustrated by the following case.

CASE REPORT

The clinical and pathological findings of this case have already been reported in detail by Greenspan (1).

History (Adm. 301722). I. K., a woman 35 years of age, was admitted to the medical service of Dr. B. S. Oppenheimer on January 30, 1929, with a five months' history of pain in the left chest radiating to the left shoulder. About four months before admission the patient was acutely ill for six weeks with fever of 103°F. and severe pain in the left lower chest, aggravated by deep inspiration. Following this illness the patient was up and about, but weakness, dizziness, and frequent rises in temperature, up to 101°F., persisted. There was mild dyspnea, but no cough or expectoration. One week before admission she became hoarse, and three days later she began to bring up blood-streaked sputum.

Examination. There were signs of aortic insufficiency, a soft diastolic murmur at the base and enlargement of the heart to the left. The blood pressure was 120 systolic and 58 diastolic. The second pulmonic sound was louder than the second aortic sound. In addition, there were râles and harsh breath sounds in the region of the left upper lobe. An X-ray examination of the chest showed a pneumonic infiltration of the left upper lobe, considered to be tuberculous, and an oval shadow just behind the pulmonary artery, interpreted as an enlarged mediastinal lymph node (Fig. 1). Laryngological examination showed the hoarseness to be due to paralysis of the left recurrent laryngeal nerve, and this was thought to be caused by pressure of the mediastinal gland on that nerve. An electrocardiogram taken at this time (Fig. 2A) revealed a tendency to left ventricular preponderance (Q3 larger than R3, but R1 not taller than R2).

Course. The patient's illness was first marked by the appearance of cough, subfebrile temperature, loss of strength, and increasing anemia.

Later a gallop rhythm and pericardial friction rub became audible. Three months after admission signs of right ventricular failure became prominent. Whereas on admission the liver edge was barely palpable, the liver now began to enlarge, and a pleural effusion on the left side, as well as ascites and edema of the dependent portions, developed. Diuretics and repeated thoracocenteses were of no avail. In spite of rest and digitalis, the signs of cardiac failure became more and more severe. Another X-ray examination showed marked increase in the size of the heart. The patient became orthopneic, markedly cyanotic and, on July 4, 1929, five months after admission, she died in circulatory failure.

Fig. 1. X-ray examination of the chest taken on February 4, 1929 shows the following: (1) marked enlargement of the left ventricle; (2) a dense infiltration in the left upper lobe extending from the first to the third interspace anteriorly (this infiltration at the time was considered tuberculous); (3) an oval shadow (arrow) just behind the prominence of the pulmonary artery interpreted as an enlarged mediastinal lymph node.

Several electrocardiograms were taken during the course of the illness. At first they did not differ essentially from the one taken on admission (Fig. 2A). Two weeks before her death, however, they began to exhibit a striking change (Fig. 2B). They now showed marked *right* ventricular preponderance (a small R wave and a large S wave in lead I; R3 taller than R2). To the clinicians, the right ventricular preponderance, together with accentuation of the second pulmonic sound and signs of right ventricular failure, suggested hypertension of the lesser circulation, but no cause for this development could be found by them. The clinical diagnosis was bacterial endocarditis of an indeterminate type, incidentally associated with pulmonary tuberculosis.

The autopsy, performed by Dr. Coleman B. Rabin, disclosed a large

chondrosarcoma of the left main bronchus. The change of preponderance in the electrocardiogram as well as all the seemingly unrelated clinical manifestations—the infiltration in the left lung, the shadow in the region of the left pulmonary artery, the hoarseness, the relentless progress of
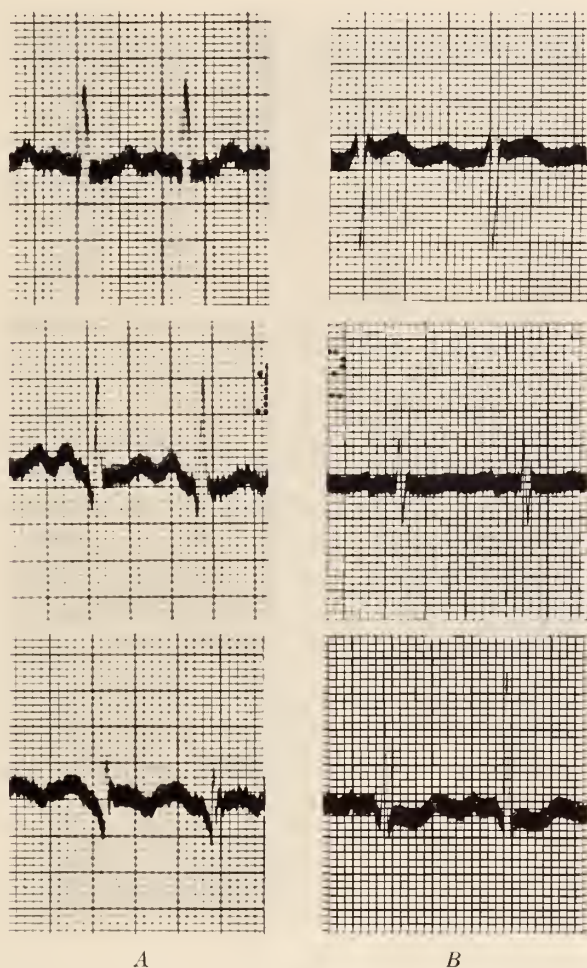
Fig. 2. (*A*) Electrocardiogram taken on February 5, 1929 shows a tendency to left ventricular preponderance (Q3 larger than R3 but R1 not taller than R2). T3 is inverted. (*B*) Electrocardiogram taken on June 22, 1929 shows marked right ventricular preponderance (a small R wave and a large S wave in lead I; R3 taller than R2). The T wave changes, as seen in this tracing, are probably due to digitalis.

right ventricular failure toward death—all were caused by the neoplasm. It had narrowed the left main bronchus, extensively infiltrated the left lung, produced an atelectasis of part of the left upper lobe and sent metastases into both lungs and pleurae. Moreover, tumor nodules had invaded

the pericardium and the myocardium. About three centimeters above
the base of the pulmonic valve, the lumen of the pulmonary artery was
found to be almost completely obstructed by a very hard tumor mass.
The right ventricle was extremely hypertrophied and the trabeculae carneae
were very prominent. The left ventricle was moderately dilated and
slightly hypertrophied. The aortic valves at their line of closure were
markedly thickened and their edges were rolled outward. For further
details of the autopsy, including the histological findings, the reader is
referred to the extensive report by Greenspan (1). The autopsy diagnosis
was chondrosarcoma of left main bronchus, closure of pulmonary artery
by neoplasm, metastases to lungs, pleurae, heart and pericardium, chronic
passive congestion of viscera and chronic rheumatic valvular disease
(aortic valve).

<div align="center">COMMENT</div>

This case is presented solely to emphasize the electrocardiographic
features, and these may now be briefly reviewed. A case of aortic insuffi-
ciency first shows moderate left ventricular preponderance (Fig. 2A),
a common finding in that type of valvular disease. In patients who,
clinically, show the dynamics of marked aortic insufficiency—high pulse-
pressure, Corrigan pulse, hyperdynamic aorta, and so-called "capillary
pulse"—the electrocardiogram usually shows high voltage and marked
left ventricular preponderance. However, when the leak in the aortic
valve is only moderate and the blood pressure about 120 systolic and 58
diastolic, as in our case, we commonly find tendency to left ventricular
preponderance or no preponderance at all. Right ventricular prepon-
derance is usually found only in case another valvular lesion, mitral
stenosis, is associated with aortic insufficiency of moderate degree. There
were no clinical signs of mitral stenosis in our case. The original electro-
cardiogram showed nothing to suggest mitral stenosis. Its P waves, in
particular, failed to show notching, the most characteristic electrocardio-
graphic sign of mitral stenosis.

While the tendency to left ventricular preponderance initially shown
by our case was no unexpected finding, the very definite change to right
ventricular preponderance constituted one of the most significant features.
This change alone should have aroused the suspicion of the clinicians
because it is quite unusual. It is observed occasionally in congestive
heart failure following acute coronary thrombosis (Master (2)). In
valvular heart disease it is even rarer. In a recent study by the author
(3), only four of one hundred and thirteen cases of rheumatic mitral
stenosis, with or without lesions of other valves, showed such change
of preponderance, and all four were cases of combined mitral, tricuspid
and aortic valvular lesions. In such a combined valvular lesion, the aortic
insufficiency may be the principal lesion at one time, and left ventricular

preponderance may be shown.   At another time, however, the tricuspid lesion may become more marked and this change may express itself in a shift to right ventricular preponderance.

In our case necropsy supplied a different explanation for the complete change of preponderance.   The tumor produced progressive narrowing of the pulmonary artery.   This obstruction to the outflow of the right ventricle increased the work of that chamber more and more, resulting in marked hypertrophy.   Our series of electrocardiograms pictures this increasing hypertrophy of the right ventricle.   The final tracing (Fig. 2B) shows the electrocardiographic signs commonly associated with enlargement of the right ventricle, high voltage (19 millivolts), and marked right ventricular preponderance.   (The change in the T wave is probably due, at least in part, to digitalis.)

Here is, therefore, another instance where the electrocardiographic signs of ventricular preponderance actually indicated an anatomical relationship of the ventricles, not merely an axis deviation.   This is usually the case when preponderance is as marked as in this instance. In our patient, such electrocardiographic signs were not produced by mere changes in the position of the heart, such as rotation, but as the result of hypertrophy of first the left and later the right ventricles, giving in the living patient a true picture of ventricular preponderance.

SUMMARY

A case of aortic insufficiency showed complete change of preponderance from tendency to left ventricular preponderance to marked right ventricular preponderance.   Necropsy revealed the cause for this change in a chondrosarcoma of the left main bronchus.   This tumor had produced progressive obstruction of the pulmonary artery which, in turn, resulted in marked hypertrophy of the right ventricle.

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PARAPLEGIA FOLLOWING MANIPULATION FOR SCIATICA; A DANGEROUS THERAPEUTIC PROCEDURE

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The recognition of the etiological factors that cause pain in the lower back is extremely difficult, and consequently the therapeutic indications are not often clear. Some of the forms of treatment are drastic and hazardous, unjustified by the present state of knowledge concerning the cause of the syndrome of low back pain. This is particularly true of nerve stretching and similarly violent manipulative procedures.

Billroth in 1869 exposed the sciatic nerve and performed an open stretching with relief of symptoms. However, this method gradually fell into disrepute because of the frequent occurrence of subsequent paralysis.

Starr in 1903 advised stretching of the sciatic nerve after other means of treatment had been tried. However, closed stretching of the nerve is not without danger, and Finkelstein reported two cases of paralysis following the procedure. Goldthwait also recorded two cases of paralysis following closed stretching for sciatic pain. One of the cases had a subsequent laminectomy at which a posterior displacement of the intervertebral disc between the fifth lumbar vertebra and the sacrum was demonstrated. In the second case the patient recovered completely without laminectomy.

Barr also reports three cases of paraplegia following manipulation under ether anesthesia. He advises against manipulations which place a severe strain on the lumbar spine.

That manipulation is hazardous can be realized when the actual steps are reviewed. Cofield uses such extreme flexion of the lower extremities that the dorsum of the foot is brought to a level with the patient's shoulder and the hamstring muscles are audibly torn. Baer does not agree with Cofield concerning the cause of the sound heard at the end of the manipulation. He thinks it is due to a slight subluxation of the head of the femur. However, he also advises stretching the lower extremities until the dorsum of the foot almost touches the shoulder.

CASE REPORT

History (Adm. 379564). M. L., male, aged 45, was admitted to the neurological service of The Mount Sinai Hospital on May 7, 1935. The patient had been well until six months before admission when he suddenly experienced a sharp pain over the left sacro-iliac joint which radiated down the left thigh and leg. The acute pain lasted three days and disappeared

after the administration of sedatives, but a dull ache persisted over the left sacro-iliac region. Two months later he experienced dull pain in the lower back and intermittent dull pain about both hip joints, more marked on the left side. There was no pain while sitting or lying down, but standing and walking caused sharp radiation of pain down the posterior portion of the lower extremities to the ankles. The pain increased in severity and five weeks before admission to the hospital he was forced to take to bed. Coughing, sneezing or any increase in intra-abdominal pressure intensified the pain and caused it to radiate to the ankles. Three weeks before admission to the hospital he entered another institution where inflammation of the left sacro-iliac joint was diagnosed. His lower extremities were forcibly manipulated under ether anesthesia and a plaster spica was applied down the left thigh. The surgeon who performed the stretching stated that he employed no undue force in the manipulation of bringing the extremity to a right angle with the torso. Immediately on recovering from the effects of the anesthesia, the patient felt tingling and numbness in the lower extremities and noticed the loss of control in his toes. This was associated with rectal incontinence and urinary retention which was accompanied by a constant dribble. The patient who had been able to urinate voluntarily before he was taken to the operating room was unable to do so thereafter. The cast was removed the same day and the patient was transferred to The Mount Sinai Hospital.

Examination. There was a complete paralysis of the right lower extremity with absent tendon reflexes on that side. There was also paresis of the left lower extremity with retention of some motion in the ankles and toes. No atrophy and no fibrillation were present. Marked muscle tenderness was noticed in the right calf. Patchy hypalgesia, hypothermesthesia, and hypesthesia from the toes up to about the fourth thoracic segment were noted. The diminution in sensation was definite only at the feet, and the uppermost level of these sensory disturbances was not clear cut. Vibratory sense was absent from the toes to the iliac crests and was diminished between the second and seventh thoracic level. There were errors in the position sense in the toes of both feet. There was spinal tenderness in the lumbar region, a distended bladder and a relaxed rectal sphincter.

Laboratory Data. The Wassermann test was negative, and no spinal fluid could be obtained by lumbar puncture. X-ray examination of the spine (May 10, 1935) showed no evidence of malignancy. Owing to the difficulties encountered in previously attempted unsuccessful lumbar punctures, a cisternal puncture was performed by Dr. Globus on May 16, 1935. The report of the X-ray examination of the spine carried out on the same day is as follows: "The injection of lipiodol (1.5 cubic centimeters) into the cistern revealed the lipiodol extending apparently from the second intervertebral foramen upward into the spinal canal and a

second small collection of lipiodol in the cervical canal itself partly at the level of the third cervical vertebra and also at the level of the sixth cervical. In the anteroposterior view the lipiodol appears on the right side of the cervical canal." No definite diagnosis was offered, but the appearance suggested the possibility of an obstructing lesion in the region of the first and second cervical vertebrae which prevented free ingress of the lipiodol and displaced the stream to the right side.

Course. At this time several neurological diagnostic possibilities were entertained—1. arachnoiditis; 2. a diffuse neoplastic process of the cord. X-ray therapy was instituted without beneficial results. Somewhat later the diagnosis of a tumor of the cauda equina was suggested and operation advised. Dr. I. Cohen then performed a lumbar puncture (May 21, 1935) by introducing the needle between the third and fourth lumbar vertebrae. Although he felt that the needle entered the subarachnoid space no fluid was obtained. He then introduced another needle between the eleventh and twelfth thoracic vertebrae and a faintly yellowish, blood-tinged (non-traumatic) cerebrospinal fluid was obtained with difficulty and this seemed to indicate the existence of block. Fifteen cubic centimeters of saline solution were then injected through the lower needle. It caused pain in the leg but no increased flow from the upper needle. The operator then concluded that a block was present below the twelfth thoracic vertebra.

Laminectomy was performed by Dr. A. Kaplan on May 23, 1935 and was described as follows:

"The incision was carried from the eleventh thoracic to the fourth lumbar. Muscle stripped from the twelfth thoracic and the first and second lumbar. The spinous process and laminae were removed. There was a certain amount of extradural fluid, but the cord did not pulsate. The dura was normal in color. The shape of the cord was normal, and there was no evidence of extradural tumor. When the dura was incised, for the whole length of the incision there was a free escape of spinal fluid. There was no evidence of a tumor although a search was made to the cauda equina. A probe was then inserted cephalad for at least three segments and no obstruction encountered. It was then decided to extend the incision, which was done, and a complete view of the cauda equina was obtained. No evidence of either inflammation or neoplasm could be obtained. A probe was then inserted caudad to this point, and no obstruction was encountered. We were at a loss for evidence of any pathologic findings in this region. Closure in layers."

Following operation slow improvement occurred. However, when examined on August 14, 1935, he displayed a rather widespread involvement of the spinal cord, and it was at this time felt that there was progressive degenerative disease of the spinal cord, and the possibility that it was caused by the manipulation was now considered for the first time.

The patient was discharged from the hospital on August 29, 1935 at which time he was able to walk about with assistance. He continued to improve, and when seen at his home two months later he was walking about without assistance and without much difficulty.

He was seen again in the Follow-Up Clinic on July 10, 1936 and an examination revealed the following:—There was marked paresis of both lower extremities, more marked on the right side, more marked in the extensors of the thigh than in the flexors, and more marked in the dorsi-flexors of the foot than the flexors. Gait was unsteady and there was a tendency to bilateral foot-drop. The right knee jerk responded with a flicker and a definite contralateral response. The left knee jerk was hyperactive, and both sides showed active hamstring reflexes. The ankle jerk was absent on both sides. There was a suggestive Babinski sign on the right side, no plantar response on the left but a positive contracture of the tensor fascia lata. Bilateral Chaddocks were obtained and an Oppenheim reflex was present on the left side. The cremasteric reflex was diminished on the left but present on the right side. The left lower abdominal reflex and a weak, right upper response were obtained. The joint sensation was impaired in the outer four toes of the left foot. Vibration was absent from the toes up to approximately the tenth dorsal segment, but here and there were areas, especially over the ankles and tibiae, where vibratory sensation was perceived, though markedly diminished. From the toes up to an indefinite level between the sixth dorsal segment and the eleventh dorsal segment there was diminution of pain and temperature sensibilities. Touch was somewhat, but least, affected. There were irregular patches of hypesthesia. It was difficult to map these out to conform to any definite anatomic distribution. Pain resulted from deep pressure over the calf muscles. The rectal sphincter was relaxed and patulous, and the rectum was filled with feces, the presence of which the patient felt.

COMMENT

Paraplegia coming on suddenly directly following manipulation under anesthesia suggests the probability that the paralysis and the other neurologic manifestations were caused by the manipulation. Highly significant is also the sudden paralysis of the bladder and rectum which could be caused only by a lesion in the cord itself, the cauda equina or in the nerve roots. A hemorrhage into the cord accompanied by swelling could well account for the subarachnoid block, as well as for the symptomatology. It has been demonstrated by reliable observers that a posteriorly displaced nucleus pulposis may simulate a cord lesion, including that of an expanding character. Such a condition is undoubtedly more common than was formerly believed, but in this instance no such lesion was noted by the surgeon who explored the vertebral canal.

Although laminectomy failed to reveal the anatomical changes responsible for the sudden paralysis following manipulation in this case, the latter is presented in the belief that manipulation, such as stretching of the sciatic nerve, a frequently employed therapeutic procedure, has its hazards which should be more widely known. Until the symptoms and physical findings of low back pain can be more accurately correlated with the anatomical and pathological factors drastic therapeutic procedures should be avoided.

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METASTATIC TUMOR OF THE MAXILLA DERIVED FROM CARCINOMA OF LUNG

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While primary carcinoma of the oral cavity occurs frequently, metastases to the jaw from distant tumors appear to be quite rare. Thus, Thoma (1), who made a recent review of the subject, has been able to collect only seven new cases. He suggests that the incidence of metastases to the jaws may be greater than is commonly assumed, and casual analysis seems to justify this contention. Secondary tumors to the jaws may be overlooked because the maxillae are usually not examined with sufficient thoroughness in roentgen-ray studies of the skeleton in advanced malignancy. Likewise, examination of the jaws is often neglected at autopsy. It is therefore probable that routine post mortem examination of the jaws in cases of tumors capable of metastasizing would disclose a greater frequency of involvement.

A metastasis to the mandible from a carcinoma of the breast is reported by Sonntag (2). Erhardt (3) mentions thirty cases of carcinoma involving the thyroid gland with metastatic invasion of the mandible.

It seems that not more than one case of primary tumor of the lung with metastatic involvement of the jaws has been recorded by Dudets as quoted by Ivy and Curtis (4). Among approximately three hundred cases of carcinoma of the lung treated at The Mount Sinai Hospital, Rabin (5) found no lesions in the maxillary bones.

This case of metastatic carcinoma of the upper jaw derived from a primary bronchiogenic neoplasm is reported because of its rarity and because of the prominent rôle that identification of the dental tumor played in establishing the diagnosis.

CASE REPORT

History (E. R., Adm. 385037). A 38 year old furrier, entered the hospital September 30, 1935, complaining of severe pain in the right shoulder and lower right thoracic region. The patient had been in good health until eight weeks before admission. At that time he suddenly experienced sharp pain in the right shoulder, followed shortly by severe shooting pains beginning in the lower spine and radiating anteriorly to the right and mid-clavicular line. The pain remained constant and was refractory to sedative therapy. As the illness continued, there developed

numbness and weakness of the lower extremities, incontinence and gradually increasing constipation. There was a loss in weight of 15 pounds.

Physical Examination was essentially negative, except for spinal tenderness at D 7, and points of tenderness over the right shoulder and right clavicle. A large number of brown pigmented nevi were scattered over the torso. Resonance of the lungs was unimpaired. The mouth had not been examined at this time.

Neurological Examination. There were flaccid paralysis of the lower extremities, absent abdominal reflexes, a sluggish cremasteric reflex and bilateral Babinski signs. Red and white blood cells were present in the urine. The Kahn test was negative. There was a moderate leucocytosis.

Fig. 1. Dental X-ray study showing necrotic area

Roentgen-ray examination of the chest disclosed a circumscribed shadow at the level of the first intercostal space suggestive of a tumor of the lung. In view of the abundance of pigmented nevi over the torso, a tentative diagnosis of melanosarcoma was made.

Dental History. On October 2nd, because of a painful mass in the upper left jaw which interfered with closure of the mouth, the patient was referred for dental consultation. At that time the following additional history was elicited. Three weeks previously the patient had visited his dentist to obtain relief for pain in the left maxillary lateral incisor region. At that time the tooth was found to be somewhat mobile and tender to percussion. The mucosa opposite the apex of the tooth showed a firm, hard swelling of moderate degree both labially and palatally. There was no clinical or radiographic evidence of either caries, pulp involvement or periapical infection. Nevertheless the tooth was extracted.

Postoperatively, the tooth socket appeared normal. The following day the patient complained of exacerbation of lumbar pain as well as increased pain in the jaw. At that time the dentist noted a small soft, scarlet mass projecting from the tooth socket.

On dental examination in the hospital, no extra-oral abnormalities were noted; neither cervical nor submaxillary glands were enlarged or tender. Some teeth were missing, several of the remainder were carious and all were involved in a marked suppurative gingivitis. The tongue was coated. Fetor oralis was pronounced.

A purplish-red mass, simulating hypergranulations in appearance, was found protruding from the socket of the left maxillary lateral incisor and extending slightly upwards over the labial and palatal mucosa. The growth was irregularly conical in shape and measured about 2.5 cm. by 1.5 cm. It was non-ulcerated, of soft consistency, non-fluctuant, and quite tender to the touch. Both in color and texture it was sharply differentiated from the surrounding tissue, which appeared normal. The adjoining teeth were slightly mobile.

A probe which could be passed readily upwards through the center of the mass, finally encountered roughened bone. Radiographic examination revealed a diffuse shadow suggesting necrotic bone radiating from the apex of the empty tooth socket for an area of 2 cm. and apparently beginning to involve the apical regions of the adjoining teeth. Material for biopsy was removed from both the exposed and submerged portions of the growth.

Biopsy Report (Dr. Klemperer). The gingival epithelium had lost its original structure and was invaded and destroyed by a highly anaplastic squamous type of cell. The cells were large, cylindrical and ovoid in shape; many were distorted. The nuclei were irregular, large and hyperchromatic. The cytoplasm contained many fine, deep-staining granules. Intercellular bridges were seen in some areas. Large areas of necrosis, hemorrhage and acute inflammation were evident. Tumor cells were seen within blood channels. Diagnosis: embryonal squamous cell carcinoma.

This lesion was now assumed to be secondary to the tumor of the lung, and the provisional diagnosis of melanosarcoma therefore was abandoned. The primary and secondary lesions were treated by radiotherapy. On October 10, the oral lesion had recurred, attaining twice its former size, and was diffuse, spongy and ulcerated, with marked extension along the labial and palatal areas. Pressure yielded a sero-purulent discharge. The general clinical course was characterized by evidence of increasing cord compression, death occurring on November 11.

Necropsy Findings. The description is restricted to the pathological alterations in the right lung which was considered to be the primary focus of dissemination:

At a point in the main bronchus one centimeter from the carina, the reddened mucosa abruptly became firm, yellow white, opaque and finely granular.   Arising from this point and spreading centrifugally into the pulmonary parenchyma was an irregular tumor mass measuring 3 by 3 cm.   Its advancing margin was poorly demarcated.   The origin of the paravertebral branch of the right upper lobe bronchus was completely lost within the tumor.   The tumor extended for the most part peripherally along the course of the axillary division of the right upper lobe bronchus.   The origin of the apical division was involved by the mass; its lumen contained yellow white inspissated material.   About 4 cm. distal to the edge of the tumor, this branch bronchus entered an irregular, ragged-walled cavity lined by yellow white and gray firm tissue.   Imme-
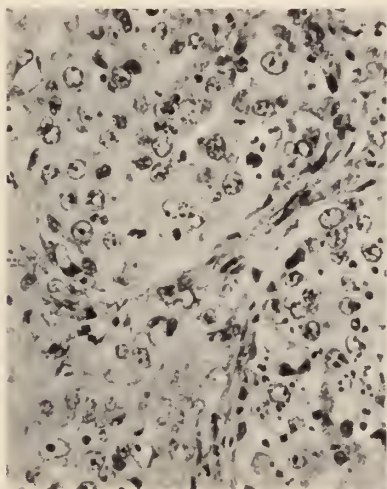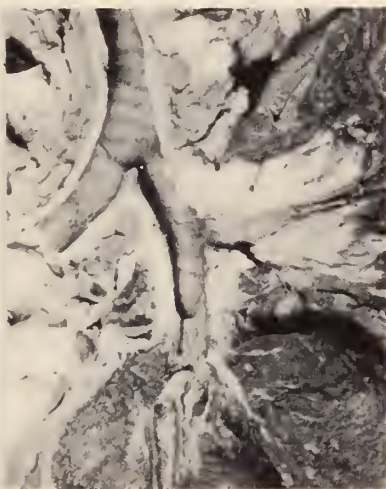
Fig. 2   Fig. 3

Fig. 2. Section from maxillary tumor
Fig. 3. Primary tumor in lung

diately contiguous to this cavity there was a 4 cm. spherical hard nodule: the center was gray. Final diagnosis: Bronchiogenic embryonal squamous cell carcinoma; secondary carcinomata to ribs, clavicle, spinal cord, skull and jaw.

COMMENT

The oral cavity is one of the most common sites of primary carcinoma, and metastatic involvement of the lung is not an unusual terminal complication of this disease.

In the case herein reported many items of evidence indicate that this sequence was reversed.   To begin with, an advanced maxillary carcinoma tends to spread rapidly over the mucosa and is rarely so sharply localized.

Moreover, in view of the fact that carcinoma is of epithelial origin and is generally situated peripherally in the jaw, the central location of this maxillary tumor strongly suggested its metastatic nature. Its origin was in the periapical bone cells of the pre-maxilla, as evidenced by the pericemental location of the pain experienced in the lateral tooth, and by the conformation and site of the area of the necrotic bone. The finding of additional osseous metastases is corroborative. Furthermore, the occurrence of the initial maxillary lesion five weeks after the onset of symptoms referable to the chest suggests most strongly the probability of its late sequence in the case. Parenthetically, one of the most interesting features of this case was the situation of the secondary tumor over the apex of an apparently sound tooth. One may speculate as to whether an overstressed occlusion with the lower opposed tooth could, through continued traumatism of the periodontal tissues, have produced a locus minora resistentia to metastasis.

The identification of the tumor in the lung as a primary neoplasm was based on the pathological features of a single mass. Metastases in the lung are generally multiple. The histological features of the maxillary tumor were identical with those in the bronchiogenic focus.

SUMMARY AND CONCLUSION

The occurrence of a metastatic carcinoma of the maxilla which appeared to be derived from a carcinoma of the lung is reported. The assumption that this tumor was secondary to the neoplasm of the lung, is based on the case history, the anatomical and pathological features and necropsy findings.

Metastatic carcinoma of the jaws is encountered rarely, and such a tumor arising from a primary bronchiogenic focus has been recorded but once in recent literature. Routine post mortem examination of the mouth and jaws in cases of malignant neoplasms may disclose that this complication is more common than has been generally assumed.

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REDUCTION EN MASSE OF A STRANGULATED HERNIA

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A hernia reduced en masse is defined by Nason and Mixter (1) as one which "consists of a displacement of the sac and its contents into an anomalous position. Despite the apparent reduction, the relation of the sac to its contents remains undisturbed." This condition, though first recognized and described by Saviard in 1702, was not accepted as a definite clinical entity until many years later. Pearse (2), however, as recently as 1931, collected from the literature one hundred and ninety such instances, including both the inguinal and femoral variety. Since then Dunn (3) has reported one case, St. John (4) has reported three cases, and Nason and Mixter have reported five more cases.

Reduction of a strangulated hernia en masse (also called apparent reduction or reduction en bloc) is thought to occur as a result of either incomplete operation, spontaneous reduction, or taxis. Eight cases resulting from incomplete operation have been described, all of which occurred before the day of aseptic technique and at a time when blind procedures were employed by surgeons who feared the subsequent development of peritonitis. The surgeon was content with dividing the extraperitoneal structures and repositing the sac into the abdomen. Sometimes reduction en masse followed this procedure. Cases resulting from reduction by taxis are by far the most numerous, and physicians have been responsible for many of these. The condition which follows this "reduction" is definitely worse than the preexisting one because of several factors: (1) the disappearance of the lump results in a false sense of security and both the patient and physician are thus encouraged to temporize and treat the condition expectantly, obviously a policy fraught with danger when dealing with strangulated bowel; (2) injury to the bowel, to the sac or both may be caused by the trauma incident to forceful reduction; (3) subsequent surgical procedures for the relief of a strangulated hernia reduced en masse are more formidable than those in a simple strangulated hernia.

Pearse explained the mechanics of reduction en masse by "the assumption of a preformed preperitoneal sac" and the subsequent conversion by taxis "of an inguinopreperitoneal hernia into the preperitoneal type." Moschcowitz (5) was inclined to regard them as preperitoneal hernias. Nason and Mixter, however, believe, as already stated, that there is such an entity as reduction en masse and that the preexistent local conditions determine the ultimate placement of the hernial sac.

Reduction en masse may be regarded as an uncommon condition, since the literature contains reports of but two hundred such instances. Pearse finds it to be "of rare occurrence, being observed in 0.0075 per cent of hernias and in 0.3 per cent of those which become strangulated. This gives an incidence of the accident in one in over thirteen thousand cases of hernia." Oddly enough, Nason and Mixter report three cases occurring in a group of six hundred and thirty-two hernias of all types, of which seventy-three were strangulated or incarcerated.

A full knowledge of the events preceding the development of this form of hernia is highly important. The commonly encountered history is as follows: a hernia of fair size and long duration becomes strangulated. It is reduced by taxis, usually with the application of a great deal of force. There is often a sudden "give," but the gurgling sound, commonly heard when the usual hernia is reduced, is absent. Concomitant with the reduction, there may be a great deal of pain. There may be no subsidence of symptoms or there may ensue temporary relief with the symptoms recurring after a variable period of time, as in the case to be presented.

The physical signs of a hernia reduced en masse depend in large measure on the stage at which the patient is observed. If a short time has elapsed since the reduction, there is little or no evidence of intestinal obstruction. If, however, the patient is observed many hours after the reduction, the classical picture of intestinal obstruction is present. Locally there may be no more than a variable degree of tenderness. Occasionally a tumor may be felt either high in the canal or in the inguinal region. The external inguinal ring is usually found to be much dilated.

There are several places in the inguinal region where the reduced sac and contents may lodge, depending on the local anatomy and the direction and amount of the force applied. If the peritoneum and the transversalis fascia in the region of the neck of the sac are not closely adherent to one another, a potential space exists. In the process of invagination, force separates the peritoneum and the transversalis fascia, thus creating an actual space. Into this space the reduced mass is lodged by force. The relation of the sac to its contents, however, remains unchanged. The neck of the sac is no longer at the internal inguinal ring, but is at the innermost portion of the mass; this condition is typified by the case herein presented. If, however, the peritoneum is loosely attached to the transversalis fascia in the region cephalad to the ring, but fairly well fixed elsewhere, then the sac, under the influence of force, will find its way into the potential space between the parietal peritoneum and the transversalis fascia at the weak point cephalad to the ring. The reduced mass will thus come to lie beneath the abdominal wall, situated mainly cephalad to the ring. The neck of the sac in this case would still be very close to the internal inguinal ring. If the laxity of attachment is mesial or lateral, the sac and its contents might be forced into one of these directions. If

the weakness is caudad to the internal inguinal ring, the sac and its con-
tents are forced along this path and come to lie retroperitoneally.   If the
attachment between the peritoneum and fascia is equally firm all around
the ring, the direction of the force might conceivably influence the ultimate
location of the reduced hernia.   In such a case, should the force applied
be great, there may occur a rupture of the sac with displacement of the
contents extraperitoneally.

The condition demands surgical interference.   A low rectus incision is
recommended as it affords easier exposure of the neck of the sac.   Such an
incision will be more fully appreciated in the event that a resection of bowel
becomes necessary.   The neck of the sac is exposed and either dilated
manually or cut.   The contents of the sac are gently reduced and appro-
priately dealt with.   The sac may then be excised from within the abdo-
men and, if warranted by the patient's condition, a herniorrhaphy may be
performed through a separate incision.   In most cases, however, it is
probably wiser to defer the plastic procedure in the treatment until some
future date as the high mortality attending cases of intestinal obstruction
militates strongly against prolonged operative procedures.

ILLUSTRATIVE CASE

History (Adm. 393132).   The patient was a 53 year old junk-shop
laborer who had had bilateral inguinal herniae for fourteen years.   The
left had always been larger and had descended into the scrotum.   He had
worn a truss over both sides for many years.   Two weeks prior to his
admission to the hospital he had been suddenly seized with severe abdomi-
nal pains and vomiting.   Pain was also present in the left inguinal region
where the hernia, having descended into the scrotum, became fixed.   The
patient made several attempts at its reduction but was unsuccessful.   He
then summoned a physician who advised a hot water bag and, should no
relief be obtained, admission to a hospital.   Nine hours after the onset of
the pain the patient pushed particularly hard and the hernia suddenly
disappeared.   He felt better shortly thereafter and passed large quantities
of gas per rectum.   He improved rapidly and remained well for about two
weeks until ten hours prior to admission to the hospital when he again
commenced to experience abdominal pain localized in the mid epigastrium
and the left lower quadrant.   He vomited repeatedly and had felt gases
moving about violently in his abdomen.   He had had a bowel movement
two hours after the onset of the attack but since then had not passed any-
thing per rectum.

Examination.   The patient was a well developed middle aged male,
acutely ill.   His temperature was 99.4°F., his pulse 74 per minute and
respirations 18.   The abdomen was flat but diffusely tender.   In the right
inguinal region there was an easily reduccable hernia.   The left side pre-
sented no hernia; the canal was somewhat large, and there was definite

tenderness high in the canal. No masses were felt. Rectal examination was negative. The white blood count was 7,900, of which the polymorphonuclear leucocytes constituted 72 per cent.

Course. An enema resulted in the passage of flatus but not stool. A barium enema revealed no evidence of organic disease of the colon. The patient was observed for the next three days, during which time he had attacks of abdominal pain and vomiting. Subsequent enemas and colonic irrigations returned stool and flatus. His temperature remained normal.

He was explored surgically three days after admission by Doctor A. J. Beller. Under spinal anesthesia a right rectus incision was made. A considerable amount of straw colored fluid was present in the peritoneal cavity. A mass in the left lower quadrant was found and partially visualized. It was seen to be a hernia reduced en masse, incarcerating and strangulating a loop of ileum. The neck of the sac was stretched carefully and the bowel liberated. About five inches of the ileum were found to be quite blue and swollen. After treating the bowel with hot saline, normal color returned and viability was evident except in one small circular area in which a definite necrosis was apparent. The entire segment of strangulated ileum was resected, both ends were closed and a side-to-side, isoperistaltic anastomosis performed. The abdomen was closed in layers without drainage.

The postoperative course was uneventful. The patient moved his bowels spontaneously on the fourth day after operation. His wound healed by primary union, and he was discharged from the hospital on the twelfth postoperative day.

Thirteen months later the patient was readmitted to the hospital and a bilateral inguinal hernioplasty was performed.

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FAILURE OF IRRADIATION OF THE SPLEEN WITH ROENTGEN RAYS IN THE TREATMENT OF ESSENTIAL THROMBOCYTOPENIC PURPURA

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Roentgen ray radiation to the spleen as a therapeutic measure in the treatment of essential thrombocytopenic purpura was first advocated by Triboulet, Weil and Paraf (1) in 1912. Since this date reports have appeared sporadically, many of them favoring this form of therapy, while a few reported no benefit. The dosage used was always small and given at irregular intervals.

Recently Mettier and Stone (2), in an attempt to establish the efficacy or inefficacy of this treatment, selected a group of cases and used larger dosage at more regular intervals. They considered their results to be striking in that there was generally a prompt response to the radiation, as manifested by a marked rise in the platelet count and the subsidence of the bleeding tendencies. A later report by Rudisill (3) described similar results in a group of seven cases and the opinion was expressed that with this form of therapy beneficial effects were quite certain.

Radiation of the spleen, with smaller dosage had been tried by us some years ago. The results were disappointing and it was discontinued. However, in view of the recent reports in which larger dosage was used with such striking results, it was decided to make another trial. Four cases which fulfilled all the criteria necessary for the diagnosis of essential thrombocytopenic purpura were selected. Because this communication is concerned solely with the results of X-ray therapy, the protocols are necessarily brief. The technique of radiation employed followed closely that of Mettier and Stone.

CASE REPORTS

Case 1. History (B.A., Adm. 395174). The patient was a 36 year old white female admitted to the service of Dr. B. S. Oppenheimer on June 29, 1936. She gave a history of prolonged bleeding following a tooth extraction ten years before. Three months prior to her admission to the hospital she began to have ecchymosis, hemoptysis, epistaxis and marked menorrhagia. There was no history of intake of drugs.

Examination. Findings were essentially negative except for numerous old and new hemorrhagic spots over the whole body.

Laboratory Data. The blood examination revealed the following: hemoglobin 92 per cent; red blood cells 4,500,000; white blood cells 10,200 and platelets 10,000. The bleeding time was 21 minutes; coagulation time 15 minutes. Tourniquet test was positive. There was no clot retraction in 24 hours.

Course. The patient was given radiation to the spleen in twelve sessions on alternate days from July 7th to August 1st with platelet counts being made at frequent intervals. On the day following the last treatment it was noted that the platelet counts showed no rise from the initial low level and the bleeding tendency continued unabated. Treatment was therefore discontinued. Subsequent hematological studies revealed no change.

Case 2. History (V. L., Adm. 395810). A 43 year old white male was admitted to the service of Dr. George Baehr on July 14, 1936. He gave a history of intermittent epistaxis over a period of fifteen years. Two days before he was admitted to the hospital he noted purpuric spots on the legs.

Examination. The findings were essentially negative with the exception of purpura on the legs.

Laboratory Data. Blood examination showed the following: hemoglobin 55 per cent, red blood cells 4,500,000, white blood cells 11,000, normal differential cell count, platelets 20,000. The bleeding time was 25 minutes. The tourniquet test was positive. There was no clot retraction in 24 hours.

Course. The spleen was radiated six times from July 18th to July 31st, each exposure being followed by a platelet count. On July 31st, after the last treatment, it was noted that the platelet count remained unchanged and there was evidently an increase in the bleeding tendency, as petechial eruptions began to recur on the extremities. Radiation was then discontinued. This patient was splenectomized on August 16th. Following splenectomy there was a prompt rise in platelets, which has been maintained, and a cessation of the bleeding tendency.

Case 3. History (A. R., O. P. D. 36-9095). This patient was a 12 year old white girl followed in the dispensary. She had a seven months history of ecchymosis and, more recently, bleeding gums. There was no history of the absorption of drugs.

Examination. Except for purpuric spots on the skin, the examination was negative.

Laboratory Data. The blood examination showed the following: hemoglobin 85 per cent; red blood cells 4,410,000; white blood cells 13,200; a normal differential cell count, platelets 20,000. The bleeding time was 10 minutes. The tourniquet test was positive. There was no clot retraction in 24 hours.

Course. The spleen was radiated eight times from January 26 to February 4, 1937, with platelet counts being made at frequent intervals. On February 5, after the last treatment, the platelet count was found un-

changed and numerous new purpuric spots were appearing. Treatment was then discontinued. Subsequent examinations have shown no change.

Case 4. History (R. B., O. P. D. 36-7049). A 35 year old white female, followed in the dispensary, gave a history of epistaxis and ecchymosis since the age of five and menorrhagia since adolescence.

Examination. Except for ecchymotic spots on the body, the findings were negative.

Laboratory Data. Blood examination revealed the following: hemoglobin 65 per cent, red blood cells 3,000,000, white blood cells 7,000, differential: normal, platelets 10,000. The bleeding time was 9 minutes, coagulation time 3 minutes. The tourniquet test was positive. There was very slight clot retraction after 24 hours.

Course. Radiation to the spleen was given on eight occasions from January 26 to February 4, 1937, with platelet counts being made at frequent intervals. After the last treatment it was found that the platelet count had remained unchanged and the patient continued to have bleeding tendencies. Treatment was discontinued.

COMMENT

The rôle of the spleen in essential thrombocytopenic purpura is unknown. Kaznelson (4) believed it to be thrombocytolytic and advocated its removal. If this was true, it might be assumed that X-ray therapy in adequate dosage could accomplish the same purpose as splenectomy. However, Mettier and Stone noted that beneficial results were apparent in their cases too soon to be attributed to the arrest of a thrombocytolytic splenic function.

In the four cases herein reported the results of radiotherapy were completely negative. Platelet counts made at frequent intervals during treatment and for some time later showed no change at any time and no decrease in the bleeding tendency was noted.

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LOUIS GROSS

May 5, 1895–October 17, 1937

It is an honor—a sad honor—to speak for you today, of our colleague and friend, who was so violently taken from us, just a week ago.

He was born here, in Montreal, forty-two years ago. He was graduated from the Montreal High School in 1911, and at once entered the Medical School of McGill University. At graduation, in 1916, he received the Holmes Gold Medal, which is awarded to the student who leads in the aggregate work of the entire course.

He spent the next five years in the Department of Pathology of the Medical School, as Douglas Fellow in Pathology, sharing in the routine work and teaching, but mainly carrying out studies on the circulation in organs, by injecting and afterwards roentgenographing them. This work, done under the kind guidance of Professor Horst Oertel, who today mourns with us the passing of his distinguished pupil, culminated in the publication, in 1921, of his classical volume, "The Blood Supply to the Heart." This work, by itself, won him a world-wide reputation, in his twenty-seventh year. During these five years began the great friendship between Dr. Maude Abbott and him.

While carrying on these studies, he managed to find time for the study of art and music. For three years, 1916 to 1919, he took up art, and, in particular, modelling and sculpture, at the École des Beaux Arts, where he won the first prize each year. At the end of the course, he was offered a scholarship for foreign study. He found time to interest himself in the mandolin, piano and violin. A couple of years ago, he began a serious study of the violin, and progressed so rapidly, that at the time of his passing away, he was a member of a good quartette.

In 1921, he went to London, to study at the Royal College of Surgeons, where he had Sir Arthur Keith as his teacher. Soon a Beit Memorial Fellowship was awarded to him, and a grant from the British Medical Association. He then continued his studies, mainly on vitamin B, at the University College.

Two years later, he came to New York, and spent a year at the Research Department of the Board of Health, studying bacteriology and immunology. At the end of that year he spent some months as head of the laboratories of the Brownsville and East New York Hospital (now the Beth-El Hospital). In 1925, he became Associate Pathologist at The Mount Sinai Hospital, in New York, and early in 1928, when only 32 years of age, Director of the Laboratories. He widely extended the scientific work of the institution. How remarkable that expansion has been is evidenced by the fact that for a number of years the staff has included over one hundred physicians, a very high percentage of whom enjoyed the opportunity for education and investigation, at the same time that they were engaged in the various clinical divisions of the hospital.

This is not the occasion on which to speak of all that he influenced, developed, and accomplished, or to speak in any detail of his own publications. For many years, he devoted himself particularly to the pathology of the heart in rheumatic fever, and of the various forms of endocarditis. In these fields there was no greater authority. In the last few years, he managed to take up what was his great desire, experimental studies on the circulation. He advanced so rapidly that when he gave demonstrations of his studies, this year, at the meetings of the American Medical Association and the Canadian Medical Association, medals were awarded to him by both organizations.

Mr. George Blumenthal, the President of The Mount Sinai Hospital, has asked me to give you the following message: "The Board of Trustees of The Mount Sinai Hospital wish to express their grief at the passing away of Dr. Louis Gross, our Director of Laboratories. We had great respect for his abilities and value and are sensible of a great loss."

He came to his tragic end while on an aeroplane trip to California. It was his expectation to make final plans there

for a new career. This was to consist of a combination of clinical work, teaching, and experimental studies. Plans were being effected for him to teach at the University of Southern California, carrying out the experimental work at the Cedars of Lebanon Hospital, and later to spend some time in the actual practice of medicine. His ardent longing, dating back many years, to deal directly with sick people was on the point of realization.

To prepare for his clinical career, he had arranged to study under the tutelage of Dr. Paul D. White, in Boston, and later with his friend of long standing, Dr. Roy W. Scott, in Cleveland. He had already spent something over a month with Dr. White, and was delighted with what he was learning from him and his associates, and with the environment. His reverence for Dr. White may be gathered from his own words. "I never had the privilege of meeting Sir William Osler, but I think that the kind of feeling I would have had for him is the same as that I have for Dr. White."

He was looking forward to the future with great pleasure. When I saw him, for the last time, about a week before his death, he was exuberantly happy. He expressed deep gratitude to the authorities at the University of Southern California and the Cedars of Lebanon Hospital, and to many friends, all of whom were welcoming him with open arms, and urging him to come to them. He expected that the climate of California and the mode of life there would enable him to work easier and better than ever before. On his last trip he stopped off to give lectures in Cincinnati and Milwaukee. All who met him spoke of his stimulating enthusiasm for the future. We all want to feel that when death came, it was instantaneous—that he died happy.

———————————

And what of the general qualities of Louis Gross? You, his Montreal early associates and his older and newer friends, know all about him! And how can one, in a short time describe the varied aptitudes and qualities of his brilliant mind!

Outstanding was his capacity for friendship, devoted and loyal friendship. He drew people to him, not by his charm and brilliance alone. He was, as Dr. Harold Segall, one of

his pupils and friends, has written, "a gallant informal gentleman." On meeting him one had the feeling of a generous soul, who was eager to be of value to individuals and to causes. He imparted his knowledge freely, but not as a superior. He was so genial, and so remarkable a raconteur, that in any gathering, everybody wanted to hear from Louis Gross. He was the life of any group that he joined.

What one felt most, however, was the radiation of truth from this man. He was bravely honest. He wanted only the truth, and he cultivated it in his work, and in his whole manner of life.

You know of his continuous interest in, and profound understanding of all things artistic. Art and music were part of his life. As not rarely happens, this man of science had the soul of an artist.

He was a deeply religious man. I have recently learned that every night before retiring, he prayed, not using the customary prayers, but such as he composed for himself.

He had a great devotion and loyalty to his teachers. Spontaneously he revered his teachers as the Talmud teaches that we should. And how happy he was when he found that a teacher expressed appreciation of any piece of work that he did. He told us of the particular joy that came to him when he received the recognition from the Canadian Medical Association, learning thereby that you, in his native country, considered that he had done something worth while. He remained on close terms with all his teachers, and they returned his devotion. Dr. Charles Martin and Dr. Maude Abbott have written glowingly of their relations to him and of the lustre that he has lent to the reputation of medical science at McGill.

He was deeply interested in Jewish affairs, and particularly in the development of the Hebrew University in Palestine. For a number of years he was a Director of the American Jewish Physicians' Committee, which is dedicated to the development of its medical department.

He was very kind to other men and stimulated them. Your own Harry Goldblatt will tell you of how Gross led him into scientific studies. And what a joy Gross had in his career and Goldblatt in that of his friend!

Younger men, without number, were aided in their ambition to carry on advanced studies. He obtained opportunities for them, assisted them in the course of their work and stood ready to be of service in their difficulties. If anything, he was over-generous in giving them credit. It is the youth of the profession that suffers the most in his departure from life.

And now the time has come, Gross, at which we should say farewell to you. But we cannot—we must not—say good-bye. You have left us in the flesh, but you are, and always will be, alive in our hearts and minds, while your name will endure in the history of medicine.

Did you not hear what your old friend, Rabbi Abramowitz read from the Psalms!

> *Who shall ascend into the mountain of the Lord?*
> *Or who shall stand in His holy place?*
> *He that hath clean hands, and a pure heart;*
> *Who hath not lifted up his soul unto vanity, nor sworn*
> *deceitfully.*

You will ascend into the holy mountain, and when you stand before the throne of glory, you will hear the happy words intoned—

Thou hast been an honest, good servant,—thou hast kept the faith!

EMANUEL LIBMAN

BOOK REVIEWS

GLOBUS, J. H. Practical Neuroanatomy. A Textbook and Guide for the Study of the Form and Structure of the Nervous System. Baltimore, William Wood & Company. $6.00.

Looking back over a span of a generation and a half, accepting the usual three generations to a century span, the reviewer envies the lot of the present day student of the structure of the nervous system. In those days there was, of course, Gray's Anatomy for gross morphology, but barring a few, and very few, reliable texts dealing with the finer structure of the nervous system were conspicuous by their absence. Even among the medical schools in the United States in these earlier years there were very meager facilities for the unusually difficult analysis of the finer details of the different parts of the peripheral, central, and vegetative subdivisions of the neural structures.

However, with Edinger, Obersteiner and then Marburg's *Atlas* the German reading student began to get some real help but the aids in English were few and far between. Barker's fine text opened the way for further excursions and soon the translations of Bing, Villiger and many other English and American works changed the whole situation so that the student tyro of today has at his command most commendable works and is thus able to cover as much or more ground than did his professors of the early period.

To consolidate this advance and also to offer first hand assistance in the study of the growing complexities in this field Dr. Globus has devised an exceptionally practical and useful work, well supplemented by the publisher's art. Here may be found an excellent compression of the earlier sources here briefly alluded to. Moreover, and this is a valuable aspect of the present work, the student is afforded the opportunity of making his own Marburg's *Atlas*, by a device of 55 perforated sheet plates with indicated rough outlines for a background. Guided by a text of simplicity and yet accurate and full, there is here offered through these semi-completed, carefully prepared drawings, a special inducement for the student to carefully fill in the details and label his observations, thus aiding him in mastering the intricacies of neurological morphology.

While preeminently a work for the medical student in the teaching of neural anatomy, there is also a valuable section devoted to clinical syndromes. Here are examples of well recognized diseases of the nervous system with well outlined histories, and detailed presentation of anatomical defects which not only impart valuable information but arouse a vital professional interest in the subject. Thus neuroanatomy, neurophysiology, and clinical syndromy are worked into unified pictures of definite pedagogic value.

After a billion years of slow progressive evolution the nervous system that finally comes to be the heritage of the human animal is marvelously adapted to the work it is called upon to perform. A deep and profound knowledge of the morphological foundations of the great coordinating parts of such a machine imparts to the study of its performance an interest of surpassing intensity and delight. Dr. Globus here presents such an opportunity.

We welcome this well gotten-up work and, as already intimated, might wish to go back to our serial sections and again take hold of the details of that 'master organ of life' which is Dr. Frederick Tilney's apt phrase in his well merited eulogistic foreword.

SMITH ELY JELLIFFE, M.D.

SOBOTKA, H. Physiological Chemistry of the Bile. Baltimore, Williams and Wilkins Company, 1937. $3.00.

In no other period in the history of science has the collaboration of chemistry and biology (including physiology and medicine) been as effective as in the last decade or two. One of the most striking illustrations of this statement is the recent development in the chemistry of bile and its recent application to the practice of medicine. Two constituents of bile, bile acids and cholesterol, stand out most prominently in this connection.

Investigations originally initiated by two independent groups of workers arrived at the unexpected conclusion that cholesterol, a normal cell constituent, and bile acids, substances which are regarded as of comparatively little value to the economy of the living organism, are built on a common pattern and that there is every reason to believe that the bile acids are derivatives of cholesterol formed in the liver which is known as the most versatile chemical laboratory of the organism of higher animals, man included. Alone this information would have been only of restricted interest, but chemical investigators have discovered that many hormones of vital importance to the organism likewise are derivatives of cholesterol. This finding suggested the possibility that the liver may play a part also in the formation of these substances and that it would not be surprising if future research should discover traces of these hormones also in bile.

Cholesterol is only one of the substances with whose function the liver is concerned. There are bile pigments, fats, sugars, proteins, nucleins whose degradation and synthesis—their balance, so to say—the liver controls. The chemistry of the intermediate stages of their degradation products has been revealed only recently and the presence or absence of these substances in bile may in the future serve as an indicator of normal or abnormal function of the liver in regard to these substances.

However, the older information always is, and should be, the foundation of newer investigations. It is therefore very fortunate that all this information has now been made accessible to every interested investigator through the volume by Harry Sobotka on the Physiological Chemistry of the Bile. The volume is not merely a compilation of the results of the older investigators but is an authoritative analysis of those results in the light of present-day knowledge. There are scattered on nearly every page many hints for new investigations by which the active worker in this field of endeavor will benefit.

The wealth of the material presented and the width of its scope may best be illustrated by enumerating a few of the chapter headings: Quantity of bile secretion, Comparative anatomy of biliary tract, Enterohepatic circulation of bile, White bile, Concentrating activity of the gall bladder, Occurrence and composition of gallstones, Choleretics and cholagogs, Emptying and filling mechanism of gall bladder, Visualization of gall bladder, Microorganisms in bile, Occurrence of bile acids outside the biliary tract, Bile acids and resorption, Immunological remarks, Pharmacological observations, etc.

The volume by Dr. Sobotka should be regarded as a very timely and a very valuable service rendered by a chemist to the medical profession at a great sacrifice of his time and energy.

P. A. LEVENE.

Shwartzman, G. Phenomenon of Local Tissue Reactivity. New York, Paul B. Hoeber, Inc., 1937. $7.50.

Translation of the Foreword: The remarkable phenomenon which Dr. Shwartzman has studied with such ingenuity and perseverance has aroused the most vivid interest among bacteriologists and immunologists. From the very beginning his discovery has been justly recognized as an important scientific development. The discovery of the phenomenon was totally unexpected, it must be acknowledged, for if there is any field which has been minutely investigated from every point of view and conscientiously searched it is that of the reaction of the organism to bacterial products. One could not have suspected that in this field secrets still remained unraveled and surprises were in store for us.

It may seem strange that the phenomenon to which the name of Dr. Shwartzman remains attached was not discovered earlier, since denoting itself by accidents, hemorrhagic in nature, it gives rise to striking and especially conspicuous manifestations, and since the conditions necessary for its reproduction are in all probability frequently encountered experimentally and in the course of spontaneous infections. In order to reproduce the phenomenon it is sufficient indeed that the products elaborated by certain microorganisms penetrate into the circulation after having acted at a given site, notably skin or mucosa. Among the microorganisms capable of developing these effects there are those like *B. coli*, which are widespread and to which the human organism is well adapted.

B. coli was employed some time ago in the experiments of Dr. Sanarelli whose very curious results could be interpreted more easily in the light of the more recent findings of Dr. Shwartzman. Dr. Sanarelli had shown that an intravenous injection of *B. coli* culture filtrate, although easily tolerated by the control animals, elicits a fatal hemorrhagic congestion in the intestinal tract of rabbits which had previously received a sublethal dose of cholera vibrio. The phenomenon of Sanarelli is closely related to the Shwartzman phenomenon, the fact pointed out in 1931 by investigations (Paul Bordet) consisting in inoculating guinea pigs, whose lymph nodes contained living microorganisms (B.C.G. attenuated bacillus tuberculosis) with products of *B. coli*, and later by the experiments of Gratia and Linz, who worked with other infections, namely, vaccinia virus. It is highly probable that these phenomena determine the pathogenesis of certain complications in the course of infections.

But I shall say no more, for it is not fitting for me to penetrate into the intimacy of the problem. In fact, Dr. Shwartzman treats it in a most complete fashion. In an impressive documentation he exposes his own experiments and those which numerous other investigators, attracted by the novelty and interest of the subject, have eagerly undertaken. In spite of the efforts spent, the problem has not yet been completely elucidated since the genesis of the symptoms observed is still somewhat of a mystery. A debt of gratitude is due to Dr. Shwartzman for having discovered the phenomenon described in this book; a debt of gratitude is also due him for having proceeded with his researches on this important problem with the great precision which he alone could achieve.

Jules Bordet.

ABSTRACTS

Members of the hospital staff and the out-patient department of The Mount Sinai Hospital are invited to submit for publication in this column brief abstracts of their articles appearing in other journals.

Thyrotoxicosis with Psychosis. J. H. Friedman and M. Kanzer. J. Nerv. & Ment. Dis., 85: 30, January 1937.

The authors review the clinical and anatomical findings in a case of thyrotoxicosis with psychosis. The clinical picture was that of an acute toxic exhaustive psychosis. The unusually rapid recovery that took place after the administration of a single dose of thyroxine, following three weeks of unsuccessful therapy with sedatives, is suggestive of a thyrotoxic etiology. From the history of the case, psychotic states appeared to be the results of an exacerbation of the existing mild thyrotoxic state by psychic and somatic traumas. The pathologic lesions in the brain indicated both acute and chronic processes.

The Experimental Nephropathies. H. Horn. Arch. Path., 23: 71, January 1937.

A review of the literature on experimentally induced lesions of the kidneys revealed that a diverse series of agents are capable of producing lesions. The abnormalities have been shown to be caused by chemical agents, bacteria or bacterial toxins, roentgen rays, renal denervation, excessive feeding and parenteral injection of proteins (including the so-called nephrotoxins).

In general, chemicals mainly effect widespread damage of the tubular system, while glomerular lesions when present have usually been focal in type. For a detailed description of the lesions encountered in this and the following groups, the reader is referred to the original article.

Repeated doses of easily filtered roentgen rays have been found to produce marked vascular lesions while single doses of lightly filtered roentgen rays induced primary tubular epithelial damage followed by vascular and glomerular abnormalities. Although tubular lesions may occur after excessive protein ingestion, the bulk of experimental evidence seemed to indicate that the degenerative alterations following such a regimen are minimal and that the only anatomical result is a work-hypertrophy of the kidney consequent to the increased excretion of protein.

Large doses of irradiated products, calcium and phosphates have been shown to have a harmful effect upon the vascular and tubular systems. In spite of the abnormalities produced by the above-named agents, it is felt that the use of such agents has but a remote application to the human disease. The value of such procedures resides more significantly in the pursuit of functional and toxicological studies. The peculiar distribution of these abnormalities, moreover, does not permit a comparison with the human disease. Of much greater importance in regard to the etiology of Bright's disease is the rôle played by bacteria, bacterial toxins and proteins (including the so-called nephrotoxins). Intimately associated with this question is that

of the relationship of the nervous system with its vascular influences. Although diffuse glomerulonephritis satisfying all the criteria required for the diagnosis of the human disease has not yet been produced experimentally, evidence at hand points to the possibility that bacteria or the products of their growth and proteins may be responsible for the inception and development of glomerulonephritis. Whether such a process is a direct result or is accomplished through the production of an altered state of reactivity, i.e., allergy or hyperergy, has still not been finally ascertained.

Mortality in Surgical Diseases of the Biliary Tract. An Analysis of One Hundred and Thirty Autopsies. R. COLP AND L. GINZBURG. Ann. Surg. 105: 1, 27, January 1937.

The causes of death in 130 autopsies occurring in surgical diseases of the biliary tract are analyzed. These are arbitrarily divided into three groups. Group I comprises those upon whom post mortem examinations were performed, in which the disease process and its complications were found to be the eventual causes of death. Suppurative cholangeitis accounted for death in 16 cases. This complication, the result of prolonged incomplete obstruction and low grade infection, ended either in multiple hepatic abscesses with or without perforation, portal or hepatic suppurative phlebitis, general sepsis or cholangeitic hepatitis. The post mortem findings represent the final result of years of operative delay, due either to lay ignorance or medical indifference. Fortunately, the importance of operative therapy in obstructive jaundice is fast being recognized. This is mirrored in the present study by the relatively few deaths from hemorrhage (only three) and the other manifestations of a prolonged obstructive jaundice. The dangers inherent in a long standing biliary duct infection with "silent stones" have not as yet been sufficiently appreciated. This fact is reflected in this series by the high incidence of death due to cholangeitic infection.

Suppurative pylephlebitis, the most fatal complication of a widespread and severe infection, was the cause of death in six cases of acute cholecystitis and in two cases of calculus cholangeitis, and contributory in five cases. When once this complication, with its multiple pylephlebitic abscesses has developed, very little can be done, and death is invariably a foregone conclusion. Diffuse peritonitis due either to a perforation of the gall-bladder into the free peritoneal cavity, a rupture of a pericholecystitic abscess, or a "durchwanderung" infection complicating acute cholecystitis, accounted for nine deaths. This represents about one-third of the anatomic causes of death occurring in acute cholecystitis. This complication affected patients of advanced years.

Group II-A is composed of the "interval" cases in which the disease at the time of operation was not threatening to life, and in which the lethal outcome could be traced either to errors in judgment or technic, or to operative complications. Diffuse peritonitis due to biliary extravasation, operative injury to viscera adjacent to the gall-bladder or the exacerbation of a latent cholecystic infection, accounted for 13 deaths. Ten deaths were ascribed either directly to immediate operative injuries or subsequent traumatic strictures of the extrahepatic bile ducts. These fatalities, approximately 10 per cent of all deaths in benign cases, are a serious reflection upon surgery because they are directly attributable to technical mistakes which probably could have been avoided.

Wound dehiscence, an almost unwarranted complication, caused death in three cases. Hemorrhage due to technical failure to secure the cystic artery or control bleeding from the liver bed was not encountered in this series. Two deaths were due to uremia, with autopsy evidence of chronic nephritis. Seven cases presented a clinical picture resembling uremia in which definite extrarenal anatomic causes for

death were found. Three cases presented a clinical picture resembling uremia but without definite renal changes evident at post mortem. These are frequently designated as hepatorenal insufficiency. They showed, however, no parallel between the degree of jaundice and the diminution of renal function. Furthermore, neither extensive degenerative renal or hepatic changes were found at autopsy. Pneumonia accounted for 11 deaths, 11 per cent of the deaths coming to autopsy. Three deaths were due to heart failure, and two to pulmonary embolism. No cases of "liver shock" were encountered following cholecystectomy.

Group II-B is composed of autopsies obtained in cases which were operated upon with a tentative diagnosis of gall-bladder disease but in which neither operation nor post mortem findings verified the diagnosis. These cases consisted of subacute yellow atrophy of the liver, non-suppurative cholangeitis (cholangeitis lenta), and biliary cirrhosis, and were undoubtedly confusing clinically. A more careful pre-operative evaluation of symptoms and findings might have avoided unnecessary surgical mortalities. Group III, comprising carcinomata of the biliary tract, consists of 28 cases. Autopsy failed to disclose the presence of visible gross metastases in the majority of malignant lesions involving the papilla and extrahepatic bile ducts. These findings emphasize the fact that these malignant lesions are worthy of an attempt at radical extirpation. The presence of fatal hemorrhage as a cause for death in these cases after a relatively minor surgical procedure emphasizes the wisdom of stage operations if the radical approach is contemplated.

Differential Analysis of Bile Acids in Human Bile from Fistulas. H. DOUBILET AND R. COLP. Arch. Surg., 34: 149, January 1937.

Frequent analysis of biliary fistula bile was made in twenty-three patients, following drainage for choledochal stones, common bile duct stricture, carcinoma of the pancreas, cholangeolitis and hepatitis. The bile was analysed for cholic acid, desoxycholic acid, total bile acids, bile acids conjugated with taurine and glycine, and total conjugated bile acids. It was found that after the release of obstruction uncomplicated by infection, the cholic acid of hepatic bile forms about 50 per cent of the total bile acid content; in the presence of inflammation of the bile ducts, cholic acid forms about one-sixth. This low cholic acid ratio indicates that the bile acids are probably absorbed by the inflamed bile ducts. In cases of acute obstruction of the biliary tract in which the gall-bladder is absent, cholic acid forms about four-fifths of the total bile acid content; in acute hepatitis, it forms about four-fifths. In all cases of pancreatitis presented here, the hepatic bile was found to contain a high percentage of bile acids.

Experimental Attempts to Increase the Blood Supply to the Dog's Heart by Means of Coronary Sinus Occlusion. LOUIS GROSS, LESTER BLUM AND GERTRUDE SILVER-MAN. J. Exp. Med., 65: 1, 91, January 1937.

Sudden occlusion of the left anterior descending branch approximately 2 cm. below the ostium of the left circumflex coronary artery in the dog's heart produces a mortality rate of approximately 50 per cent. In dogs weighing approximately 15 kilos surviving more than twenty-four hours (average one week), an infarction is produced which almost invariably measures 5 by 5 cm. on surface. Following coronary sinus obturation, such secondary sudden occlusion of the left anterior descending branch is followed either by no infarction or by a reduction in the size of the infarct. The success of the procedure, quite apart from the mortality rate, depends upon the completeness of the coronary sinus obturation. On the other hand, sudden and complete coronary sinus obturation by itself is associated with a high operative mortality and apparently does not affect the mortality rate following subsequent sudden left anterior descending branch occlusion. Partial persistent obturation of the coronary

sinus, however, is in itself associated with a low operative mortality. Furthermore, its experimental production in dogs appears to lower the mortality rate following subsequent sudden occlusion of the left anterior descending branch and to diminish the extent of the infarction.

The optimum method of producing partial coronary sinus obturation was found to be the injection of escharotics around the vessel. This manipulation is simple, can be performed in the dog within approximately twenty minutes, and does not lead to appreciable pericardial adhesions. Increase in the nutrition of the myocardium is noted one week after the experimental procedure. Although no experiments employing sudden left anterior descending coronary branch occlusion were carried out sooner than one week, there is available anatomic evidence that, within possibly twenty-four hours after coronary sinus occlusion, a dilatation of the vascular bed occurs. In subsequent experiments attempts will be made to determine whether this early vascular dilatation is adequate to compensate for subsequent sudden left anterior descending branch occlusion. A discussion is given of the results following various coronary sinus occlusion procedures in which it is indicated that it is desirable to produce a partial or gradual occlusion in order to lower the mortality rate both of the initial procedure as well as of the subsequent sudden arterial occlusion. Experiments thus far reported on cardiopexy operations are lacking in evidence that they are associated with appreciable improvement in the vascular nutrition of the myocardium.

Mental Symptoms in Cases of Subtentorial Tumors. M. KESCHNER, M. B. BENDER, AND I. STRAUSS. Arch. Neurol. & Psychiat. 37: 1, January 1937.

In one hundred and twenty cases of verified subtentorial tumors, mental symptoms were observed in fifty-six. Many patients presented mental changes so slight that unless one searched for them with great care, they escaped detection. The mental symptoms were milder and less complex in children than in adults; this may have been due to the greater technical difficulty in eliciting slight disturbances in children. Mental symptoms in cases of subtentorial tumor were much milder and less complex than those in cases of supratentorial tumor. Crude visual hallucinations of the type usually observed in cases of supratentorial tumor may occur in cases of infratentorial tumors. They were present in four patients. The early appearance of profound and complex mental changes, especially those involving disturbances of memory and intellect, in a patient whose only evidence of tumor of the brain is intracranial hypertension, is in favor of localization of the tumor above the tentorium; in this sense the mental picture in a patient suspected of having tumor of the brain may perhaps be of some localizing value. Too much reliance, however, is not to be placed on the mental picture for this differentiation. If studies with the use of air are indicated in a patient with such a condition, especially if the intracranial pressure is greatly increased, it is safer to resort to ventriculography than to encephalography by the lumbar route.

Attempted Solution of Renal Calculi by Dietetic Measures. G. D. OPPENHEIMER AND H. POLLACK. J. A. M. A. 108: 349, January 1937.

Following the preliminary reports of Higgins on the successful solution of renal calculi in human beings by a high vitamin acid ash diet, the authors treated a series of patients by the method he outlined. The diet employed is described and the theoretical principles involved in the use of Vitamin A and an acidifying diet discussed. Simultaneous pH measurements of the urine from both kidneys illustrate the difficulty of obtaining a sufficiently low pH in the pelvic urine of a stone-bearing kidney when such a kidney has diminished function or is infected with alkali-producing, urea-splitting organisms. Of 52 patients treated, 27 were on the diet from 6 to

16 months with an average of 11 months. Twenty of these maintained a sufficiently low mean bladder pH (5.2 or under). There was no evidence of partial or complete solution of the radio-opaque calculi thus treated! The authors were unable to confirm Higgins' claims.

"Retrograde" Abdominal Hysterectomy with Avascular Morcellation for Large Fibroids.
I. C. RUBIN. Am. J. Obst. & Gynec. 33: 137, January 1937.

The technique is described of removing by bloodless morcellation through a subumbilical incision large myomatous uteri reaching the upper abdomen. The uterine vessels are ligated on both sides, or first on one side, followed by amputation of the cervix. The lower end of the detached fibroid-bearing uterus can now be delivered into the wound where it is reduced in size by morcellation until it is entirely removed. The advantages of this procedure are that the smaller incision prevents large hernias and the fibromyomatous uterus in situ during the operation avoids intestinal trauma, lessens shock and promotes postoperative comfort comparable to that following a vaginal hysterectomy over which it has, moreover, the general advantages of a laparotomy.

Fractures of the Femur Treated by the Russell Traction Method. M. A. SALLICK.
Surg. Gynec. & Obst. 64: 103, January 1937.

Some modifications are made in the femoral traction method devised by Russell, and a routine is outlined to facilitate its efficient use. Experiences in a series of 29 cases treated by this method are analyzed and discussed.

Good results with Russell traction can be expected only if careful attention is given to details in the use of the apparatus. Correct adjustment of the angles of pull is necessary to obtain maximum traction efficiency. The danger of overpull is emphasized. Preservation of good joint function even after prolonged periods of suspension is a uniform and striking feature of this method. The comfort of the patient and the facility of nursing care are factors to be mentioned in its favor.

In the author's experience this method is particularly advantageous for intertrochanteric and subcapsular neck fractures. Its use is also advocated for fractures involving the upper and middle thirds of the femoral shaft. In the treatment of the lower third of shaft fractures, however, Russell traction is unsatisfactory and its use in these cases is not recommended.

ANNOUNCEMENT

Through the kindness of Doctor Alfred Meyer, consultant physician to The Mount Sinai Hospital, provision has been made whereby graduating interns and a limited number of members of the Out-Patient Department may be placed on the mailing list of the Journal of The Mount Sinai Hospital for a period of one year, on payment of fifty cents (to cover the mailing expenses).

Those who are interested may apply to Dr. J. H. Globus, Editor-in-Chief of the Journal.

JOURNAL

OF

THE MOUNT SINAI
HOSPITAL

NEW YORK

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Introductory Note

This special number of the Journal is dedicated to

DR. EDWIN BEER

to mark the completion of thirty-eight years of active service at The Mount Sinai Hospital. Its pages carrying messages, penned in his honor by distinguished surgeons and physicians, both here and abroad, bear witness to the high esteem in which he is held.

The friends, colleagues and pupils of Dr. Edwin Beer, an acclaimed leader in his chosen field, welcome this opportunity of conveying to him their appreciation and sincere good wishes.

Edwin Beer.

EDWIN BEER AND BASE HOSPITAL NO. 3

HOWARD LILIENTHAL, M.D.

[New York City]

He made a noble appearance in his military uniform—always a distinguished looking man, even as I first remember him. This was while I was operating in an abdominal case and, happening to glance toward the head of the table, there stood a dignified intern-anesthetist of athletic build and classic features. Many years later, when recognition of his outstanding original work had come to him, and his renown in neurologic and genito-urinary surgery ran even, there came the World War.

Edwin Beer, naturally patriotic, joined the Army in the spring of '17 and was ordered to Fort Benjamin Harrison, near Indianapolis, for instruction in the military side of medicine. When he was set to work counting dirty laundry as part of the preparation for War Surgery he must have wondered if he had not made a mistake. His task surely had no relation to the award of the Gold Medal, ten years later, in Brussels, by the Societé Internationale d'Urologie, when he was the first to receive this distinction, though the medal had been in existence for a number of years. Nor had this menial task anything to do with his decoration in 1936 with the Gold Key of the American Congress of Physical Therapy. This commemorated his invention of intravesical procedures for the destruction or removal of certain diseases by electrical means. The discovery avoids the dangers of approach through the abdomen or the perineum, and saves many lives and much misery and pain.

The Commanding Officer of Base Hospital No. 3, the Mount Sinai Unit in France, was Major Michael A. Dailey, now Lieut. Colonel. He was thoroughly versed in what may be called Medical Engineering, and he lost no time in converting the unfinished French Asylum for the insane into a military institution of modern equipment suitable for the care of any type of illness or injury. It had formerly been a monastery of the Carthusians, an order long active in religious affairs. The name, la Chartreuse de Vauclaire, was still its descriptive title. Some of its twenty or more buildings were of mixed Gothic architecture of great charm with gardens and cloisters all of which were used for the multitude of departments necessary for a plant of this kind. Beside the hospital ran a little winding tree-bordered river. Before the end of the war many temporary structures were added so that at one time we accommodated twenty-eight hundred patients with no actual overcrowding.

Major Beer, a leading figure in our group, was selected by the Commanding Officer to assist in arranging the wards for the efficient distribution of the various kinds of disease or injury, thus facilitating the transportation of the sick and wounded as they arrived by hospital trains. While waiting for patients from the battle-front there was hard work of all sorts for the enlisted personnel; but rest and recreation were indispensable, and the usual athletic sports of young vigorous men came as a matter of course. Major Beer, himself a former athlete, became interested in organizing games and other contests. He returned one day from a trip to Limoges with a football for the boys ("men" is the correct Army term). There should have been motion pictures when he illustrated fancy passes and graceful drop-kicks.

Recognizing his ability and good sense outside his profession, he was at one time detailed to map some of the surrounding country and to gather information concerning land and structures which might be of use in emergency as hospitals or for other military purposes.

In his spare time Beer studied French and carefully read the maps of the war progress. He wrote many letters home, using carbon paper to avoid repetition, an example which I was glad to follow. Upon our first arrival at our destination he and I sent cable messages to our wives at home and we used about the same form: it ran—"Safe arrival getting settled well love", and the name signed. Long afterward we found that our distrustful government, fearing prying eyes and suspicious of a possible code, had censored the messages so that the only word received was "love" over the signature.

"Next week I'm going to give myself a birthday party," Beer announced one day, "and you are all invited to be my guests," thus reversing the usual custom of such feasts. "It will be a dinner at the Puits d'Or," the quaint little inn of Mme. Patinet in Montpon sur l'Isle, the metropolis of our hospital, and about three miles down the road. "The K. O.[1] and all the officers are invited." There would be about thirty at the table, and we put ourselves on our social honor to make some grateful and appropriate gesture. I'm not sure but it seems to me it was Captain Jacob Asch, D.D.S., whose plan was carried out. The idea was to surprise our host at the end of the dinner with the presentation of a great birthday cake and candles with all the usual fixings and formalities. Our baker, great flat-footed, toothless Radovic, whose infirmities had been overlooked by Major Walter Brickner[2] because he was an expert of the oven, was given the com-

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[1] Commanding Officer.

[2] Our greatly lamented friend and comrade, Dr. Brickner, did a great service to The Mount Sinai Hospital by his conscientious and understanding selection of the corps-men of our Unit. I doubt that his wisdom and diplomacy were ever appreciated at their full value. Barbers, chiropodists, plumbers and steam-fitters, carpenters and those of other trades were represented and, as in the case of Radovic,

mission to produce a work of artistic merit. The huge confection came into existence, its decorations elaborate in design, its frosting of brilliant poly-chromatic floral and geometric pattern. It was amazing that the great spatulate fingers of our baker could fashion such an intricate and beautiful object. The bright blues, yellows, reds and greens were made from dyes of the bacteriological laboratory.

The Puits d'Or was a simple little country village inn with a tiny garden which, with its vines and willows, when seen through the window, became suddenly picturesque and paintable. Here was the Well of Gold itself where the wine was cooled; and what we drank that night must have taxed the capacity of this natural refrigerator. The smoke of good Ameri-can Quartermaster's cigars, so envied by our Gallic comrades, cast a tender blue haze over the scene and, with the moka and liqueurs, a cake was set before our host. Clearly affected, he gracefully expressed his appreciation and at once proceeded to divide the gift among his guests. But after the first section through the frosting the blade refused to go farther; it had struck—a block of wood![3] With flushed face Major Beer characterized the joke as in the worst possible taste when, at just the right moment, the stately, candle-covered product of our own bakery made its appearance and all was forgiven. With "He's a Jolly Good Fellow" the birthday party ended and, after traveling the miles back to Vauclaire, we were ready for the duties of another day.

Beer had the good fortune to be sent as an observer to the Front and, on returning to the Base, he warned me not to seek the arduous service at or near the fighting lines. I was indignant. An old camper and hunter in our Northern Woods at home to be dissuaded because of possible physical inconvenience! When my own Team 39 went forward with Walter Brickner and W. A. Kellogg we were stationed at Evacuation Hospital No. 8, eight miles from Verdun during the activities in the Argonne, St. Mihiel and other sectors. There was nothing in the life which seemed to me an actual hardship though, of course, there were annoyances and in-conveniences—rats beneath the tent floor, for example. And there was danger of an occasional bomb from a plane, not necessarily aimed at our hospital. How I might have endured trench life I cannot say.

Dr. Beer's team was ordered to the American Hospital in Paris (Neuilly) where it did splendid work. With him were nurses and two officers, Leo Meyer and Edwin Sternberger. Living in Paris had many advantages;

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occasional physical defeats were overlooked so that we might acquire men of excep-tional ability. Throughout our stay in France and almost from the beginning, other hospitals, some of them very influential, tried to steal (?) our men to the annoyance of Major Dailey who usually managed to have them returned to us.

[3] Who originated this I have never been able to discover. There was the frosted cover of many hues and forms, but the cake was not quite so large as the one we had all seen, and there were no candles.

Fig. 1. Major Beer's operating team

Fig. 2. Major Beer's operating team with gas masks and trench helmets

it brought one near the center of things, and there were opportunities for fraternizing with many officers of our allies. There was, for example, the Cercle Interalliée with its informal Club life. It occupied an impressive mansion with picturesque grounds in the heart of the city. As an occasional guest of the Cercle I cannot help, even now, envying Dr. Beer his recollections, but I am glad to have had my war surgery in the Zone of the Advance.[4]

Major Beer returned to the United States in December, 1918, after the war. For the past twenty years his unremitting and successful labor for the development of urologic surgery has been acclaimed by all who have followed medical history. When his term of service in the hospital wards has been completed and the well-beloved drudgery of daily rounds is over we may look forward to more of his scientific discoveries and to new methods and devices for the amelioration of suffering and the prolongation of life.

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Some years ago when the time came for the selection of a skilled surgeon and adviser for the writer, Edwin Beer was chosen, as a matter of course. It was certain that nothing would be overlooked which scientific knowledge and proficiency could promise; and that an old acquaintance beginning with the contact of Attending and Intern would add to the confidence of the patient and the moral obligation of the surgeon. Both predictions have been fully justified.

[4] J. A. M. A. 72: 839-843, Mar. 22, 1919.

EDWIN BEER: HIS CONTRIBUTIONS TO UROLOGIC SURGERY AND LITERATURE

BRANSFORD LEWIS, M.D., B.Sc., F.A.C.S.

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In reviewing the scientific contributions of Edwin Beer, one is fairly amazed at their number, at their exalted merit and practical value, and finally at the great variety of subjects that he has studied, described and oriented. While urology has furnished the basis for the greater part of his work, both operative and literary, he has gone afield for original contributions on other topics: gastro-intestinal pathology, diseases of the liver, the spleen, the spinal cord and miscellaneous subjects. All of his writings have been serviceable in a practical way, and have on that account been studied by practitioners and students alike. They all show the logic of the philosophic mind that surveys his subjects in a broad, inclusive way, relieved of the myopia that afflicts certain specialists of limited vision and restricted thought.

A further striking impression that one gets from reviewing Dr. Beer's writings is that they are ever in the forefront of surgical progress, whether they relate to the diagnosis of obscure urologic affections (1, 2, 3, 4), the bearing of radiography or fluoroscopy in diseases of the urinary tract (5, 6, 7, 8), or to the radical strides made in recent years in the diagnosis and reclamation to health of children affected with obscure urinary conditions that formerly were practically ignored and permitted to go on to a lethal end because of the fears of parents and practitioners to pursue a logical course of investigation and relief, such as has been developed by Beer and other urologists in modern times (9, 10, 11, 12).

That the child is the father of the man, pathologically speaking, appears in Dr. Beer's recognition of the fact that contraction at the vesical neck (11), often first observed in adult or middle life, has really been present and steadily growing since childhood, and might, with diagnostic acumen and energy, have been recognized and relieved in infancy, forestalling the destructive effects of years of back-pressure and its attendant evils.

This "ounce of prevention," in the writer's opinion, has proved one of the most valuable steps of progress that has been made in modern urology —which essentially and really is a modern structure.

Dr. Beer's dissertations on renal lithiasis (13), uric acid showers (14, 15, 16, 17), phosphaturia (18), the operative removal of stones in the kidney (19), and progress in nephrectomy and nephro-ureterectomy (16, 20, 21,

22, 23, 24), are all valuable in the extreme and depict the views of the thinker, as well as the surgeon.

His expressions in comparing open operative methods of removing ureteral stone with the less heroic cystoscopic manipulations (25, 26), are fair to both sides of the argument and exhibit a balanced judgment not always observable in such discussions.

In the decade of 1905 to 1915, when the surgical world was learning the vast import and direct bearing of functional renal tests on the mortality of operations, Dr. Beer did not fail to add his quota to the general research that was going on.   This appears in his papers of that period, on "Blood Cryoscopy in determining the functional activity of the Kidneys" (27); "The value of the indigo-carmin test as an aid in the diagnosis of partial and total ureteral occlusions" (28); "The phloridzin test" (29); "The interpretation of functional renal tests with special reference to the significance of minimal excretion of 'phthalein and indigo carmin" (30); and "The value of functional renal tests properly interpreted" (31).

His several contributions on urinary tuberculosis deserve especial mention because of their sensible trend and the fact that the deductions submitted were based on the very large urologic service of The Mount Sinai Hospital and the meticulous care with which they were observed and followed.   They embraced the following titles:

"Stone and Tuberculosis of the Kidney" (32);

"The use of Tuberculin in the diagnosis of obscure conditions in the genito-urinary system" (33);

"The significance of ureteral tubercle bacilluria" (34);

"Chronic tuberculosis of the Kidney" (35);

"The diagnosis and treatment of chronic tuberculosis of the Kidney" (36);

"Discussion of paper on the patho-genesis of renal tuberculosis" (37);

"Delayed wound healing following nephrectomy for tuberculosis" (in collaboration with Leo Edelman) (38).

While the surgical work and contributions of Dr. Beer, already mentioned, may well serve as landmarks, indicating his keeping apace with or, in many instances, leading in the rapid steps of progress in the urology of recent years, without doubt his crowning achievement in originality and practical surgical service was rendered in 1910 when, with characteristic modesty, yet masterly conviction, under the title "Removal of Neoplasms of the Urinary Bladder," he gave to the profession a first report on the treatment of such growths with the Oudin high-frequency current (Journal of American Medical Association, May 28, 1910)—a method that was destined to revolutionize the surgery of benign vesical tumors, to win the approval and applause of the medical profession the world over, and the gratitude of thousands of sufferers from such growths.   He was in a

peculiarly advantageous position to render judgment on the outstanding value of such a comparatively innocuous method because of his large personal experience with the open surgical attack on bladder tumors in The Mount Sinai Hospital Service (39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50).

Experience with the method soon demonstrated its utility, its efficiency in benign growths, and its freedom from the many drawbacks and failures of the older mutilating resections, as well as the greater assurance it gave against recurrence. Also, it was soon learned that such promising results could not be expected from its use in malignant growths, although many operators still place faith in the value of fulguration (successor to the Oudin application), with or without the use of radium in malignant tumors.

At any rate, urologists since 1910 have never ceased giving Beer a full meed of appreciation and praise for his epochal discovery and application of this method. He has described it fully in subsequent papers (51, 52), to which he later added a Monograph on "Tumors of the Urinary Bladder," published by William Wood and Company in 1935.

It is evident that Dr. Beer, through his numerous and able contributions to surgery and literature, has earned an exalted place in the Urologic Hall of Fame.

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TEAM WORK BETWEEN SOCIAL SERVICE AND DR. BEER

FANNY LISSAUER MENDELSOHN, B.S., R.N.

[From the Social Service Department of The Mount Sinai Hospital, New York City]

Any word of tribute which we might utter would be inadequate to express the esteem in which the social workers hold Dr. Beer. His sympathetic understanding of the social problems which confront his patients, his kindly approach, and his humane manner towards all make it a privilege and pleasure to work with him. The patients whom Dr. Beer has helped through the medium of the Social Service Department are too numerous to mention, but I should like to cite a few examples which will indicate to some extent the harmonious relationship and the excellent cooperation between him and the social service of the hospital, as well as the splendid results which ensued.

C. H., Male, 14 years (Adm. 320558). C. was born with a congenital deformity which necessitated extensive and repeated surgery. He was subjected to the first operation, for exstrophy of the bladder, when he was 7 years old. His home conditions were pitiable. The parents were separated, the father serving a prison sentence for non-support, while a Jewish welfare agency was assisting his mother. In the course of the many years during which he was being treated, a number of medical-social problems presented themselves. There were periods when convalescent care or the providing of proper diet was necessary; there was constantly a need for funds for transporting the patient to the clinic; there was the problem of school adjustment; and there was the need of giving his mother and teachers instructions for proper care. Throughout these years, Dr. Beer was always ready to give constructive advice to the social service worker and to assist her in making and carrying out the best plans for this boy's welfare. At the present time C., who is now 14 years old, has repaid for all these efforts by developing into a bright, handsome boy, enjoying normal ways of living.

H. R., Male, $3\frac{1}{2}$ years (Adm. 414879). H., $3\frac{1}{2}$ years old, has been a patient in the Children's Ward on four occasions with the diagnoses of recurrent pyelonephritis. Here the social problem was not that of finances, since the family income was adequate. It was mainly of proper supervision, since the mother's emotional imbalance caused by the child's condition made it impossible for her to properly care for him. With the aid of Dr. Beer's advice to the parents and of his recommendations to the

social service, the problems growing out of the child's illness are being met by the parents with a better understanding and place much less nervous strain upon the mother.

M. A., Female, 8 years (Adm. 345360). Since the age of 4, M. has been under Dr. Beer's care in the hospital and the out-patient department. The child has an anomalous kidney with infection and pyuria. The family, which is large, has been on relief, and was unable to provide the required care and special diets. Dr. Beer, fully understanding the home situation, recommended to the social service such steps as would enable us to devise ways and means to assist the family in looking after the little patient.

M. A., Male, 12 years (Adm. 319238). M., during his long illness with tuberculosis of the kidney, was a patient of Dr. Beer. The parents of the boy, although intelligent and cooperative, were in constant need of guidance and advice regarding the child's care and treatment. Dr. Beer displayed deep interest in the unfortunate boy and, to serve him better, gave generously of his time to counsel the parents about various matters, even so far as to formulate detailed plans for their migration to California in order to assure a better future for the boy.

EXPERIENCES WITH SURGERY OF THE SPLEEN; REPORT OF TWO UNUSUAL CASES*

ROBERTO ALESSANDRI

[Rome, Italy]

Edwin Beer has been one of the pioneers in surgery of the spleen. I am glad to pay him honor on the thirtieth anniversary of his surgical activity, by reporting a few particulars of my experience in this field.

I. EXPERIENCES WITH SURGERY OF THE SPLEEN, ESPECIALLY WITH SPLENECTOMY AND WITH LIGATION OF THE SPLENIC ARTERY; INDICATIONS FOR THESE OPERATIONS

Among the one hundred and one cases treated up to June 1937 there were seventy-two splenectomies, one splenic resection, and sixteen operations for ligation of the splenic artery. There were twelve cases of injury by firearms in war and in peace. In one instance I was able to perform suture of the spleen. In other cases I had recourse to tamponade; once I applied pressure to the injured splenic vein. There were seven cases of splenic cyst. These included one large post-traumatic blood cyst, treated with marsupialization, and six echinococcus cysts. The latter were treated occasionally by marsupialization, but preferably by incision of the cyst cavity, extraction of the chitinous membrane, and immediate closure, as is customary in similar lesions of the liver.

Ligation of the splenic vessels, especially of the splenic artery, seems to have been performed first in the sixteenth century by Viard in a case of movable spleen; the method was studied experimentally by M. Malpighi in 1649. After a few cases treated by different techniques and under different and poorly justified indications, the method was carried out by Stubenrauch (1921) with exact technique and more precise indications. It was subsequently repeated for different splenic lesions and with varied results.

I treated the subject at length in a general article which I published in 1935 (1), reporting eight cases operated on by me, and subsequently in the International Journal (2), in communications to the Academy of Medicine of Rome (3), and again in 1937 (4), assembling, as I have said, sixteen cases. To avoid repetition I refer the reader to these articles for the details.

It has been stated by certain authors, including Beer in his article

* Translated from the Italian by Saul Jarcho, M.D.

of 1928 (Annals of Surgery), that ligation of the splenic vessels is more
dangerous and more difficult than splenectomy. I wish to insist here
that this conception is incorrect.

If ligation is attempted on single vessels of the hilum it can indeed be
difficult and also incomplete or dangerous, since the vessels are terminal
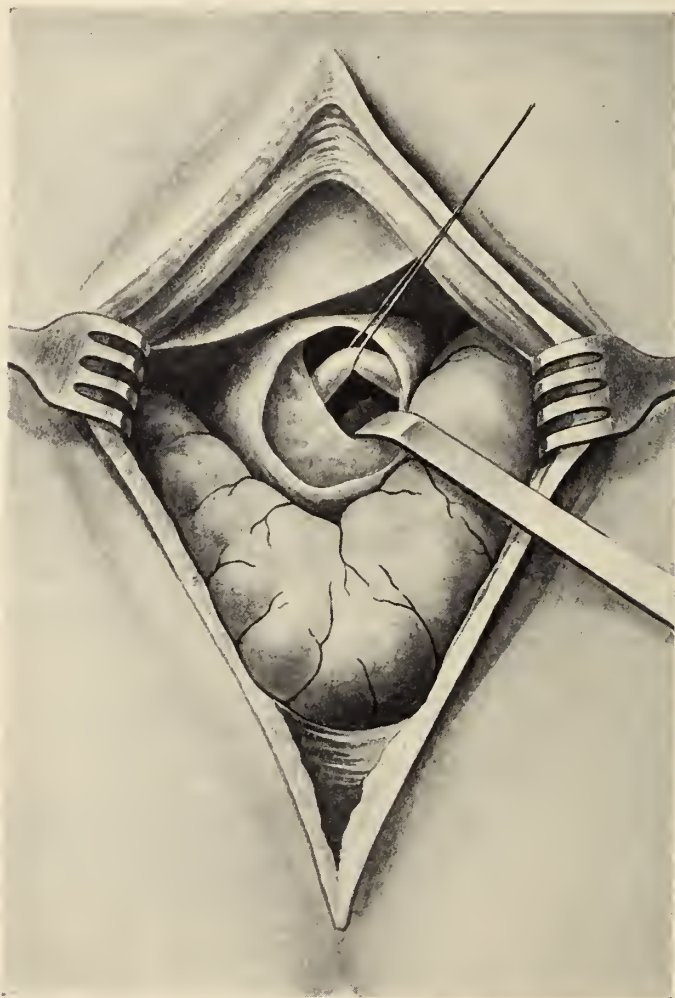
Fig. 1 (see text)

and necrosis of the spleen may be produced. However, if ligation is made
at the site of election—i.e. at the superior margin of the pancreas (Fig. 1)—
either by simple ligature or preferably by cutting between two ligatures,
the procedure is almost always very simple and can be performed under
local anesthesia, even on patients who are seriously sick. The only
possible difficulty, one which I have met in a case of thrombosis of the

splenic vein, is the development of a compensatory venous circulation with many tortuous and dilated vessels which cover the artery and impede its exposure.

There are no dangers of any sort if the vessel is well exposed and the surgeon assures himself that it is the splenic artery (which may be greatly enlarged in cases of marked splenomegaly). When it is desirable to do a splenectomy the operation is made much easier if the artery is ligated first, as is done by Leonte and Lötsch.

Since a compensatory collateral circulation is always present, the danger of massive splenic necrosis does not exist. Experimental studies
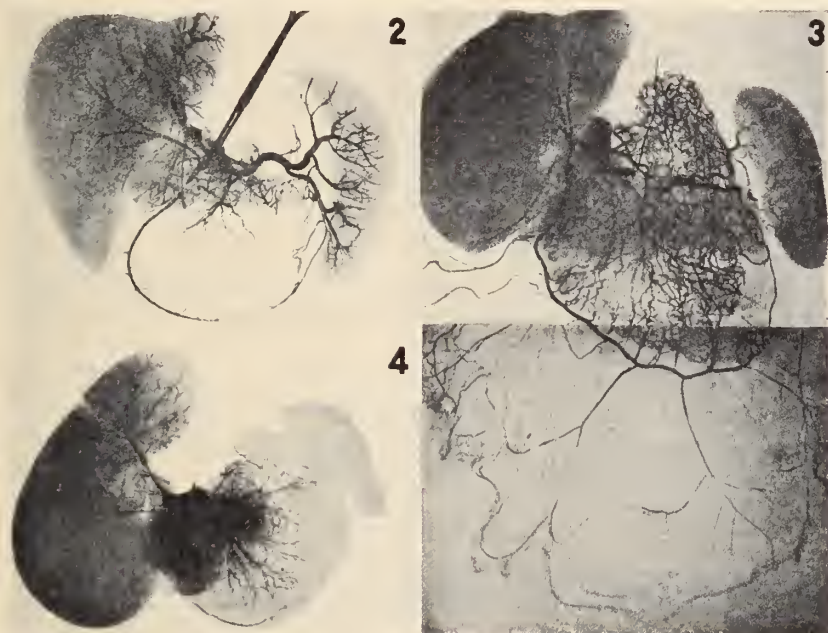
FIGS. 2, 3 AND 4 (see text)

bearing on this point have been numerous. I shall mention only those of C. Rossi and of Valdoni, which have shown this clearly; the operative results have brought confirmation. After the good results in two cases of hemolytic icterus in which I performed ligation of the splenic artery, P. Valdoni, in my clinic, made exact animal experiments in, and careful post mortem studies of, the collateral circulation. The results were amply confirmatory and I take pleasure in submitting a few illustrations from this work (Figs. 2, 3, and 4).

But the indications represent the most important consideration, and in this respect clinical experience is decisive, as Beer himself clearly stated at the close of his article: "Even though at the present time it is difficult to define accurately the indications for splenectomy in many of these cases

and even much more difficult to determine when ligation of the splenic artery should be used instead of splenectomy, still the more carefully the cases are studied and the more completely they are reported, the sooner will the clinician be able to decide on the value of these two procedures, and in general upon the indications and surgical attack in these varied clinical pictures."

I have already discussed this in the two articles aforementioned; I shall now summarize the more important data. My sixteen cases include three of hemolytic icterus, two cases of purpura haemorrhagica, one case of metrorrhagia of puberty with signs of thrombopenia, three cases of lymphoid leukemia, one myeloid leukemia, one thrombophlebitis of the splenic vein, three cases of splenic anemia with signs of hemolysis, and two cases of Banti's syndrome.

A disease in which ligation of the splenic artery has often been employed is thrombopenia, or Werlhoff's disease, but I repeat here what I have stated previously, that I consider splenectomy always preferable in these cases. The spleen is almost always of normal size or slightly enlarged, and is usually free from perisplenitis or adhesions such as might impede mobilization and splenectomy. The seriousness of the cases is usually due to the severe anemia; however, with the aid of transfusions the operation can be executed successfully. Only in acute cases is it advisable to wait, if possible.

I have performed ligation in two cases of patients in extremis on whom I operated at the insistence of the physician and with very little hope. The first was a woman aged 47 dangerously sick after many hemorrhages; the second was a man of 60 who was seriously stricken and had signs of cerebral hemorrhage. In neither instance did the operation prevent death. In the first case autopsy showed hemopericardium and gastric hemorrhage; in the second there were two subdural hematomas.

In the case of a girl aged 16 who had obstinate metrorrhagia and whose general condition counterindicated splenectomy, transfusion followed by ligation of the splenic artery produced rapid improvement; this will make it possible to perform splenectomy if the symptoms should recur.

The same principle has guided me in the use of ligation in cases of hemolytic icterus, in which it had already been mentioned by others, but never applied. I carried this out for the first time in 1928 (5).

Here the indication seems to me to be much greater, although I recognize that splenectomy is preferable. But in these cases the spleen is often huge and often adherent and hard to remove; the patient's resistance may be enfeebled by severe anemia and intense hemolysis. Moreover, in these cases transfusion is often useless or even harmful, since it is frequently followed by hemolytic crises (Greppi).

As I have stated above, even if ligation does not cure the disease, it

may nevertheless lead to improvement sufficient to permit splenectomy if the symptoms recur. This happened in one of my cases.

In cases of lymphoid and myeloid leukemia, according to my experience, ligation is to be avoided. I have tried it because it is an operation which even very sick patients can tolerate. I was also stimulated by Payr's results in similar operations on the artery (Drosselung). However, in four cases treated in this way there was one prompt fatality; in the others the disease was uninfluenced.

Indications which I consider adequate are afforded by: congestive and sclerotic-congestive types of splenomegaly, especially in cases in which definite contraction is produced by adrenalin, and above all in those cases of splenic anemia (Banti's syndrome), not better identified, in which there is a hemolytic component; splenomegaly with gastric hemorrhages, not only those cases with hepatic cirrhosis of the ordinary or Banti type in which the hemorrhage is due to abnormal development of esophageal and gastric veins consequent to portal obstruction or the cases of thrombophlebitic splenomegaly accompanied by gastric and cardial varices, but especially the cases in which the portal, splenic, or even intrasplenic veins (Grégoire and Weil) are not occluded by thrombi. In thrombophlebitis splenectomy appears unjustified. If thrombosis is absent it would seem logical to ligate the splenic artery and thereby reduce the entry of blood into the spleen.

I consider the operation indicated in cases of splenogenous gastric hemorrhage, which are occasionally complicated by gastric or duodenal ulcers (Alessandri, Greppi, Pallasse). In these cases the hemorrhages may come from the ulcers but can also be independent of them. In my case hemolytic factors were present. In Pallasse's case death occurred through perforation of an ulcer which did not bleed. In Bombi's case neither ulcers nor varices were present.

It is uncertain whether the gastric or duodenal ulcers occurring in cases of splenomegaly are a mere coincidence, as believed by Nicolosi and Di Stefano, or are attributable to vascular lesions due to stasis or to neural disturbances of the gastric and duodenal mucosa (Greppi). It is also possible to have hemorrhage without ulceration (Bombi). This has been attributed to toxic lesions of the splanchnic nerves or of the sympathetic nerves about the splenic artery (Frumosan)—an explanation which is contradicted by experimental studies (Nicolosi); even here it seems necessary to assume a state of lability of the gastric vascular network secondary to the splenic lesion (Greppi). In all these cases ligation of the splenic artery may be useful and I should consider it justified. In my case I resected the stomach and duodenum and ligated the splenic artery; Bombi has done the same. In other cases gastrojejunostomy and arterial ligation have been performed. In general the results have been good but clinical experience is as yet inadequate.

II. REPORT OF TWO UNUSUAL CASES; LARGE SPINDLE-CELL SARCOMA; ERYTHREMIC SPLENOMEGALY WITH COMPLETE SPONTANEOUS RUPTURE OF THE SPLEEN

Of the cases in which I have performed splenectomy I wish to give brief reports of two which I consider important for various reasons. The first was a case of huge tumor (spindle-cell sarcoma). The second was a case of rupture of an erythremic spleen.

The rarity of primary and metastatic tumors of the spleen is well known. The most common are the so-called splenomata or splenocytomata; it is still doubtful whether these are true tumors or systemic lesions.

True sarcoma is quite rare; it is said to occur most often in the young. However, Moynihan reported a case in a woman of 50 years. My patient, a man of 52, was a colonel in the Army. He had no past history of syphilitic or specific disease. He had gone through the war unwounded, and had not had malaria or any other disease of importance, or any traumata. After the war he began to have discomfort which was poorly localized in the left flank. The symptoms consisted not of pain but rather of a sense of weight or pressure; this drew the attention of physicians to the spleen, which was found to be enlarged. Soon the costal arch became elevated and the swelling inclined downward. The spleen rapidly increased in volume but there was no impairment of the patient's general health and the blood picture was nearly normal. There was a mild degree of anemia, no leukocytosis or leukopenia and no change in the red cell series. Various treatments were ineffective especially antiluetic treatment; this was administered despite the negative history and the absence of serological evidence of syphilis. Radiotherapy was similarly ineffective.

The splenic swelling was tremendous. Splenic dulness reached as high as the fifth rib in the mammary line. The spleen filled the entire hypochondrium and epigastrium; it crossed to the right of the median line and almost touched the iliac crest. There was no ascites. The palpable portion was hard, with a rounded margin and no incisura; it was slightly mobile and mildly tender.

Roentgen examination revealed the presence of non-aneurysmal dilatation of the thoracic aorta including ascending and descending portions, as well as the arch. The entire vascular structure showed vigorous expansile pulsation. The heart was elevated and slowed (by the subjacent large spleen). The base of the left chest expanded very little and was slightly obscured by a small effusion and adhesions. There was nothing to suggest tumor metastases in the lung fields.

The urine contained faint traces of albumin, a few leukocytes and occasional erythrocytes.

From time to time the patient's temperature was elevated. This occurred with increasing frequency.

In November 1925, the patient being admitted to the Clinic, I decided to do an exploratory operation in order to ascertain the diagnosis and to attempt radical treatment. On December 3 I made a left perirectal incision about ten centimeters long. There was no free fluid in the abdomen. The spleen appeared very greatly enlarged, globular, with large bosses, firm and elastic; it was of gray-red color and quite mobile.

The fever which was previously present now diminished. Having completed the examination and established the diagnosis, I felt that the indication for splenectomy was confirmed. On December 27 I reopened the wound, prolonging it downward and laterally and connecting it above with an oblique incision toward the median line. In this way I had plenty of space and easily mobilized and removed the voluminous spleen. The pedicle was ligated in parts, and then the small vessels and the splenico-phrenic ligament were tied. Primary union occurred.

The spleen was large and weighed thirty-seven hundred grams. The surface was firm and elastic, with large bosses. The cut surface was gray-red and compact. Microscopical examination showed the presence of interlaced bundles of long spindle-cells having long nuclei. These were at first interpreted as sarcomatous spindle-cells. Another pathologist regarded them as muscle cells and as such I reported them in a brief communication to the Congress of the International Society of Surgery at Rome (1926). However, a subsequent and more precise examination reestablished the earlier interpretation of the cells as sarcomatous spindle-cells, unequal in size and having an irregular or sometimes double nucleus.

After the operation, which was well tolerated, the patient developed left-sided hydrothorax which was drained twice, six hundred cubic centimeters being removed on January 20 and one hundred cubic centimeters on February 17. On March 31, the wound having healed by primary union, the patient was dismissed in good general health.

A few months later he began to weaken once more. He now developed ascites and a palpable epigastric mass referred to the left lobe of the liver. He declined rapidly, and died on June 23, 1927.

The autopsy disclosed the presence of a single large metastasis in the left lobe of the liver. This lesion had the same microscopical structure as the primary tumor.

Aside from the rarity of the case, I take interest in the finding of an isolated metastasis in the left lobe of the liver. This proves once again the direct circulatory connection between the spleen and the hepatic lobe. In cases of Banti's disease Deaver and others repeatedly observed that hepatic lesions of the cirrhotic type quite often begin in the left lobe and are always more advanced in that lobe.

The second case is particularly important in two respects: first with regard to the mechanism of rupture of the spleen with hemorrhage in

two phases and almost complete separation of the organ into two halves; likewise the immediately favorable result of emergency splenectomy; second the favorable effect (up to the present time) on the patient's general health and blood picture, despite the fact that the indication for splenectomy in cases of erythremic myelosis is still under debate.

The clinical history may be summarized as follows: The patient was a woman aged 28 years who had had no previous illnesses. She had been married for three years. Her first pregnancy, two years ago, had run a normal course and was followed by normal parturition and lactation. The second pregnancy was uneventful until the eighth month (December 15, 1936). Since then she had had asthenia, dyspnea, and intense pallor. In the Obstetric Clinic marked hepatosplenomegaly was found, as well as severe anemia resembling pernicious anemia; also edema of the lower extremities and paroxysms of severe dyspnea. Normal spontaneous parturition occurred on January 25, 1937. There was no serious loss of blood. The child was alive and healthy.

The anemia increased and the patient was transferred to the Medical Clinic, January 28, 1937. She now had marked edema of the face, lower extremities and sacrum. The skin and mucosae were extremely pale. There was mild cardiac enlargement, and an anhaemic murmur was audible at the apex. The liver edge was three fingers' breadth below the costal margin. The spleen reached upward to the seventh interspace and continued downward four fingerbreadths below the costal margin. It gradually increased in size.

Examination of the blood: red blood cells 770,000; hemoglobin 19 per cent; color index 1.35; reticulocytes 3 per cent; white blood cells 7,400; polymorphonuclear leucocytes 72 per cent; eosinophiles 1 per cent; basophiles 1 per cent; lymphocytes 22 per cent; monocytes 4 per cent.

On February 10, after a transfusion of three hundred cubic centimeters and proper medical care, the erythrocytes numbered 2,400,000, the formed elements being not otherwise changed. The following nucleated types of red cells were found: erythroblasts (orthochromatic and polychromatophilic) 12 per 100 white blood cells; basophilic erythroblasts 19; proerythroblasts 2. Sternal puncture revealed marked erythropoietic reaction. The bone marrow was extremely rich in cells, almost all of which were of the normoblastic series; predominant among these were very young forms such as proerythroblasts, basophilic erythroblasts, and many mitotic forms. There was a distinct megaloblastic and reticulo-histiocytic reaction. Splenic puncture showed the presence of an erythroblastic reaction.

After a few days there was aggravation of the anemic syndrome and tenderness in the hypochondrium and left flank with increasingly clear signs of rupture of the spleen. On February 14, 1937, the patient being most dangerously ill, a transfusion was performed and was followed by the removal of a large spleen (twelve hundred grams) divided into two almost

equal parts by the rupture of a laceration. The splenic bed was packed
and the abdominal walls were partly sutured. A second transfusion was
given immediately after the operation. Healing occurred by second in-
tention. There was also an abscess in the left side due to phlebitis.

Repeated preoperative examinations of the peripheral blood made it
possible to exclude the diagnosis of disease of the leukopoietic system.
The diagnosis of pernicious anemia was excluded by the reticulocytosis,
the absence of macrocytosis, the absence of megaloblasts and hyper-
chromatic megalocytes, and finally by the hepatosplenomegaly. More-
over, glossitis and sternal pain were not present. It was not possible to
study the gastric changes.

Against the diagnosis of hemolytic jaundice was the absence of micro-
cytes and of abnormal erythrocytic fragility.

The first few postoperative days were characterized by the hematologic
signs of typical erythroblastic reaction following splenectomy; these
soon subsided.

In view of the microscopical findings in the sternum and spleen, the
morphological findings in the blood, and the type of anemia, the case must
be considered one of disease of the red cell series (erythremic myelosis?).

Sections of the spleen showed marked reduction of the lymphoid
apparatus. Remnants of follicles were present. There was much blood
in the sinusoids. The pulp cords were hyperplastic; there was prolifera-
tion of endothelial cells. There was partial myeloid metaplasia and an
abundance of cells of the erythroblastic series.

After the operation the patient's general condition improved markedly.
Most striking was the marked increase of erythrocytes. Red blood
cells 4,250,000; hemoglobin 52 per cent; color index 0.6; white blood cells
7,500. The blood picture remained at this level after March 1937.
Immature red cells were still found in the peripheral blood but were not
numerous.

The liver has diminished noticeably. Recent advices (October 1937)
indicate that the patient is still in good general health.

With regard to the first of the points mentioned above it may be asked
what was the mechanism of the splenic rupture. This was apparently
spontaneous. However, it is well to remember that the patient had given
birth to a child six weeks previously. It does not appear that there were
any signs of internal hemorrhage or of splenic pain during labor. How-
ever, we know that these large spleens, softened by myeloid hyperplasia,
may easily develop small or large foci of subcapsular hemorrhage which
may remain circumscribed and almost asymptomatic. The gradual
increase in size of the spleen, as observed postpartum in the Medical
Clinic, is important and suggests enlargement of a subcapsular hematoma.

However, a few days before the serious crisis and operation the spleen
was punctured with a large needle for diagnosis. We may imagine that
this produced a recurrence of the hemorrhage and, by piercing the capsule,

may have initiated the laceration. The latter started with vague symptoms which were rapidly aggravated. The diagnosis was doubtful; internal hemorrhage and perforated ulcer were considered; of the latter condition there had been no antecedent history. The surgeon, Dr. Jura, was called at once; in view of the possibility of serious intraperitoneal hemorrhage, he operated at once. A transfusion had been given. The surgeon found the spleen almost completely separated into two parts (Figs. 5, 6, and 7) and removed it, saving the patient, who was almost in extremis.

The second point is even more important. This type of splenomegaly, which Di Guglielmo (1923) first pointed out as the erythropoietic analogue of leukemia and pseudoleukemia, is at present being discussed not only with regard to its nature but even with regard to its name. Di Guglielmo refers to it as erythremia, while others call it erythremic myelosis.
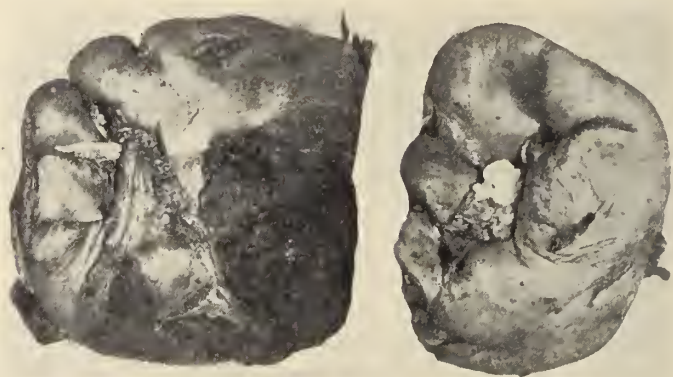
Fig. 5. Spleen separated into two parts

Essentially it consists of anemia with splenomegaly—frequently very great—with almost exclusive involvement of the red cell series. As I have said, this might constitute a lesion analogous to leukemia, according to the ideas of Di Guglielmo. By analogy with typical leukemia, the changes may consist of an increase of cells of the red series (polycythemia, Vaquez's disease). However, the qualitative changes are of particular importance; they may affect the red series (erythremia vera or propria) or may also affect the leukocytes or platelets or even all three (global erythremia).

The typical form of the disease has been studied mainly by Italian authors (Di Guglielmo, Fontana, Omodei-Zorini, Canale, Storti, and others). It is characterized by a systemic hyperplasia of the erythroblastic series with tendency to arrest of cellular maturation and with passage of immature red cells into the circulation. Clinically there is always a more or less well marked anemia, usually hypochromic or hyperchromic, almost always with moderate or severe splenomegaly (seventeen

hundred grams in Di Guglielmo's case, twelve hundred grams in our own case after removal of blood). The spleen usually contracts well with adrenalin. The liver is also almost always enlarged.

A fundamental characteristic is hyperplasia of the red elements. At times this is observed in the peripheral blood, at times only on histological
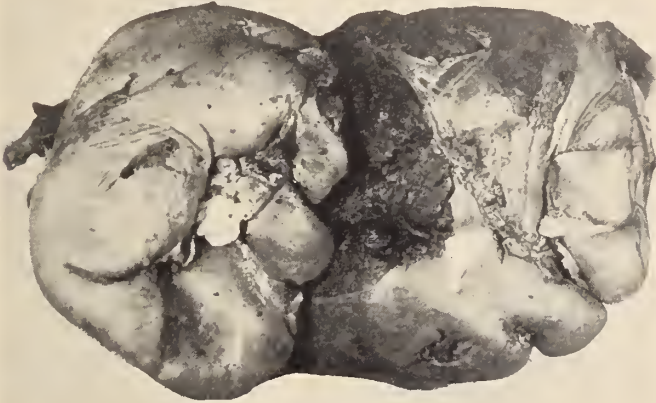
Fig. 6. The two parts put together

Fig. 7. Cut surface of the spleen

examination. In the circulating blood there are changes in the red cell series, usually qualitative rather than quantitative. The presence of nucleated red cells is not sufficient for the diagnosis. If there are basophilic nucleated cells of the red series and if these preponderate over the polychromatophilic and acidophilic cells and if mitoses are observed,

the picture is typical. There is also a disproportion between the picture of anemia and the presence of immature red cells in the circulation. If the latter are very numerous, the diagnosis is certain.

Histologically there is in general a systemic hyperplasia of the bone marrow, which is completely transformed into erythropoietic tissue, with scant involvement of the leukopoietic or thrombopoietic systems. However, there are also cases with myeloid hyperplasia (Esposito) or even with complete aplasia of the bone marrow (Storti). Also the erythroblastic metaplasia of the liver and spleen can be very variable and different from that in leukemic cases.

Cooley's anemia, which has been studied especially in America, may represent a similar lesion. Its characteristics are: more or less severe and predominantly hypochromic anemia; poikilocytosis; constant and marked erythroblastosis with predominance of the less mature cells over the more mature types, i.e. a tendency to arrested maturation; normal or increased number of leukocytes; excessive hemolysis; splenomegaly; and osteoporosis.

From the therapeutic and especially the surgical point of view—for I shall not now insist on concepts of pathogenesis or on hematologic minutiae, or on diagnosis, since in the medical field the discussion is still open— operative intervention is not favorable. In fact, splenectomy is considered counterindicated. There are, however, in the Italian literature two cases (Fontana-Pettinari and Stefanutti) of good operative result, the cure having persisted for years. It is true that certain observers have objected that these are not cases of genuine erythremia. In the case operated on by us, in which splenectomy was performed not because of medical indication but because of the emergency of rupture, there seems no possible doubt of the diagnosis, considering the findings in the bone marrow, circulating blood, and spleen. The doubt which arises above all through the improvement (I may say the cure) of the patient can come only with an erythroblastosis of pregnancy. However, it has seemed important to report the case because it is an interesting addition to the understanding of this form of erythremic myelosis, which is still under discussion, and to the question of the possibility and usefulness of operative intervention.

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SUBCAPSULAR NEPHRECTOMY*

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There are certain pathological changes in the perirenal tissue, which may render difficult lumbar nephrectomy; and which may lead to very serious complications, if one attempts the mobilization of the kidney in the accepted way of enucleating it between the capsula propria and the fat capsule. This difficulty is encountered particularly in the attempt to ligate the hilus vessels. Chronic inflammations, stones or suppurations are frequent causes of fibrous thickenings of the perirenal fat and may lead in the process of dissection to tearing of the peritoneum, injury of the intestinal wall and other serious conditions, and sometimes to fatal results. Hence, for some time the subcapsular enucleation of the kidney was recommended in cases of such difficult nephrectomies. The mobilization of this organ is accomplished by the incision of the capsula propria. By doing this it is not only possible to avoid the above mentioned hazards, but technically a much simpler and safer operation is thus attained. However, in spite of these advantages subcapsular nephrectomy has as yet not found the general application, which it deserves according to my experience. It is also technically not performed with any degree of uniformity and it is for this reason that it will be discussed in some detail.

The various textbooks dealing with surgery of the kidney do not discuss very extensively the technic of this operation. Albarran, in his classical textbook of operative surgery, recommends an extracapsular enucleation of the kidney in cases in which the kidney cannot be mobilized because of too short a pedicle. After decapsulation is performed, the vessels should be grasped by clamps and the pedicle should be isolated after incision of the capsula propria. Kümmel emphasizes the difficulty or even the impossibility of attaining an isolated ligation of the vessels in the case of short pedicles ("shortneck" kidneys). In his extensive work on "Surgery of the Kidney," Papin has high praise for the subcapsular nephrectomy, especially in the presence of a kidney fistula. Edwin Beer, with an experience of more than two hundred nephrectomies, found the subcapsular nephrectomy very valuable. He rightfully sees a great advantage in this method, since it excludes the application of clamps and ligatures en masse to the pedicle and thus the danger of injurying the colon or duodenum is excluded.

Feodoroff, too, uses the intracapsular enucleation for the operative treatment of nephrolithiasis, if the organ is markedly immobilized by adhesions.

I, myself, as an assistant to my teacher, O. Zuckerkandl, have seen subcapsular nephrectomy performed frequently and successfully, according to the technique described by Lichtenstern in his textbook on urological surgery. He says: Kidneys which, because of a long standing suppuration, are "baked in" a mass of dense perinephritic adhesions, thus acquiring short and thick pedicles, present difficulties in mobilization. Therefore, in his opinion, nephrectomy is only possible by means of the intracapsular method.

It may be seen from the aforementioned quotations, which are by no means complete, that subcapsular nephrectomy is widely known and often performed; some use it in cases of complicated nephrolithiasis, others in fistulas, pyonephroses, or secondary nephrectomy. This method always proved to be advantageous, but its indications are as poorly defined as are its technical steps. I myself have used regularly for many years subcapsular nephrectomy in suitable and in a steadily increasing number of cases and proceed in the following way:

THE SURGICAL STEPS

After incising the lumbar musculature one approaches the renal fat and, according to the degree of pathological changes in the latter, especially in cases of thick adhesions, it is best to cut immediately into the capsula propria and to roll it up from the kidney in toto to the level of the pedicle of the renal vessels. If one is dealing, as is often the case in such instances, with a short neck kidney, the finding of the vessels is difficult and, what is even more important, their isolated ligation is impossible. For this purpose I cut around the rolled up capsula propria renis on its interior aspect, as close as possible to the sinus renalis and perpendicular to the direction of the vessels; I employ short circular cuts or make a half circumference incision at the ventral aspect of the organ (Fig. 1), until it is possible to reflect the capsular tissue upwards and downwards without further cutting. This can be done without difficulty. By means of this dissection the vessels as well as the renal pelvis and the ureter are exposed, so that these structures in the further course may now be ligated, each of them separately, without clamps and with the avoidance of the undesirable ligature en masse (Fig. 2). This done, the removal of the kidney is performed as in any nephrectomy.

By following this technic in the course of more than twenty years, I never had any serious accident during a nephrectomy. Almost never was it necessary to apply a ligature en masse at the stalk of the vessels; I, certainly, was never forced to leave in the hemostat. Also injury to the vena cava or to the intestinal wall never occured.
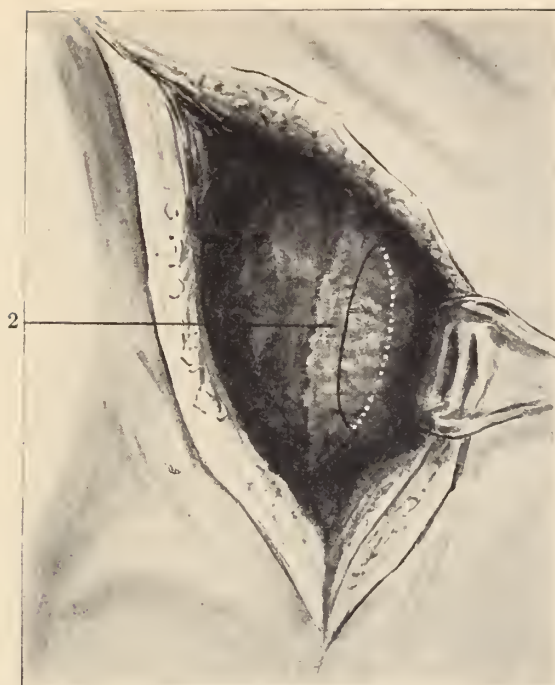
FIG. 1. The reflected capsula fibrosa of the kidney—internal aspect
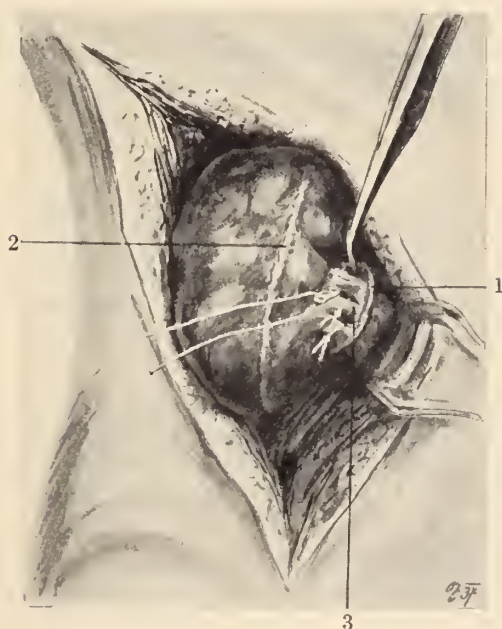
FIG. 2. (1) The distally reflected part of the capsula propria renis. (2) Part of the capsula propria renis reflected towards the kidney. (3) Hilus vessels and ureter isolated, each separately.

The intracapsular enucleation is of advantage for another reason. In the course of the mobilization of the upper kidney pole by means of blunt digital separation outside of the capsula propria the adrenal may easily be injured or erroneously removed. This will cause disturbing hemorrhages; such accidents are impossible if the subcapsular dissection is used.

Under these circumstances one must ask why the subcapsular nephrectomy is not always performed when pathological changes in the perirenal tissue make the extracapsular operation difficult. The only contraindication to this method is present when, because of an existing pathological process, the removal of the capsula fibrosa also is necessary. This is especially true in cases of malignant tumors, where the extension of the tumor from the renal surface towards the capsule makes such a dissection impossible. A second contraindication is found in tuberculosis of the kidney, where a nodular dissemination on the surface is frequently present with which one must avoid getting into direct contact. The two conditions, tumor and tuberculosis, are probably the only diseases of the kidney, which may make desirable the sparing of the kidney capsule, and its simultaneous removal together with the kidney. As far as common infections are concerned, I have never needed to remove the indurated, thickened capsule specially; it is possible by means of a light tamponade, even if it is left in, to obtain a satisfactory healing of the wound.

I am aware of the fact that I have not devised a new operative method, but at most added a new detail in the technique which has served me well in the subcapsular extirpation of the kidney. I consider it especially important to reemphasize the advantages of this operative method, as I have the impression that it should be used more frequently than it has been in the past.

CONCLUSIONS

1. The subcapsular nephrectomy is recommended as the *method of choice* in all cases in which extirpation of a kidney with indurated thickening of its adipose capsule is indicated and in which there are other difficulties in the mobilization of this organ. The only exceptions are tumor and tuberculosis of the kidney, when the removal of the capsula propria is desirable.

2. The subcapsular operation prevents with an almost one hundred per cent safety a dissecting injury to the peritoneum, pleura and intestine.

3. This operation offers the possibility for isolated ligation of the vessels of the stalk, so that ligatures en masse are avoided, which aids the healing of the wound.

4. The subcapsular dissection may be performed usefully also in some cases of tumor and tuberculosis when accompanied by marked adhesions, as the secondary extirpation of the capsula propria may subsequently be carried out without great difficulty.

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A CASE OF PLASTIC RESTORATION OF THE PENIS*

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A 21 year old student, native of a far eastern country, was sent to me with the following history:

Six months before, he became the victim of an attack motivated by jealousy. Under the cover of night, he was assailed in his own apartment and anesthetized with chloroform. His penis was then amputated just above the scrotum. Several hours later he was brought to a doctor's office almost completely exsanguinated. Timely and proper surgical attention to the wound saved the man's life. Yet, the diabolic plan of the assailants was completely realized. The artificially produced impotentia coeundi in the presence of normal or even increased libido profoundly depressed the young patient. He first consulted the physicians of his own country, then, taking a trip around the world, consulted many other European and American physicians searching for advice as to how to regain the potentia coeundi.

I was able to make photographic and cinematographic records of the operation which I performed in several stages. Discretion, however, will not allow me to publish these pictures; the accompanying diagrammatic sketches will suffice to describe the several steps in the plastic restoration.

Figure 1 shows the condition in which the patient was found at the time he was brought to me. At the upper border of the scrotum there was a deeply retracted area from which the urine was discharged during micturition and from which it was spilled over the scrotum. Figure 2 is sketched after a drawing in Tandler's Topographic Anatomy, and illustrates the anatomical relationships at the site of the stump.

The operation was aimed at the elongation of the penis and was accomplished by the following two measures:

1. The urethro-rectal fascia, which continues into the raphe of the bulbo-cavernous muscles (Figures 4 and 5), was severed. It was then possible by vigorous traction, using a blunt instrument, to bring out the entire bulbus urethrae by at least three centimeters and to fix the bulbus in this new position by deep sutures which attached it to the surrounding tissues.

2. A further elongation of the stump of the penis was achieved in the following manner. The left corpus cavernosum penis was dissected from
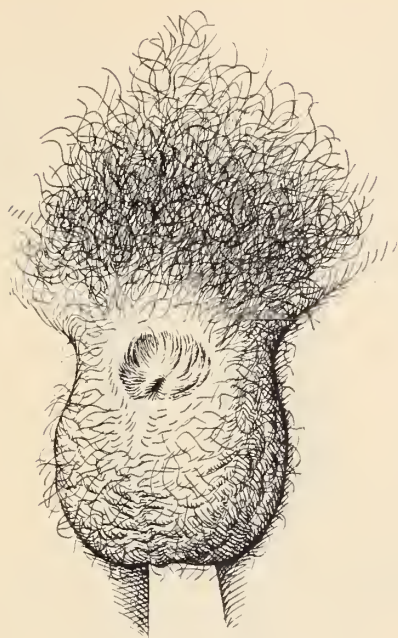
FIG. 1
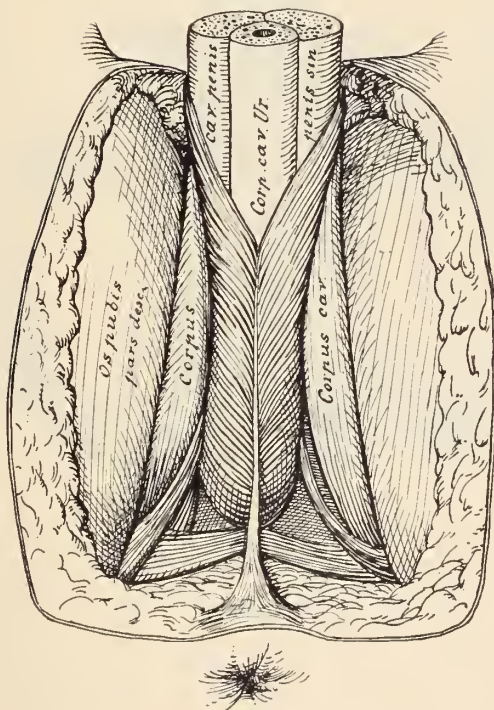
FIG. 2
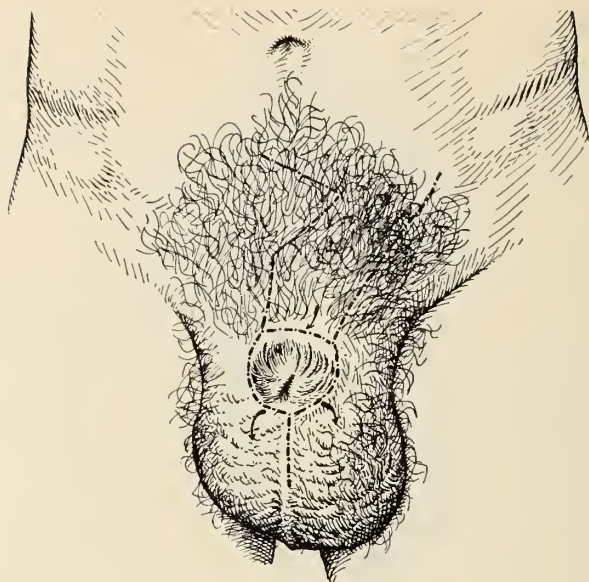
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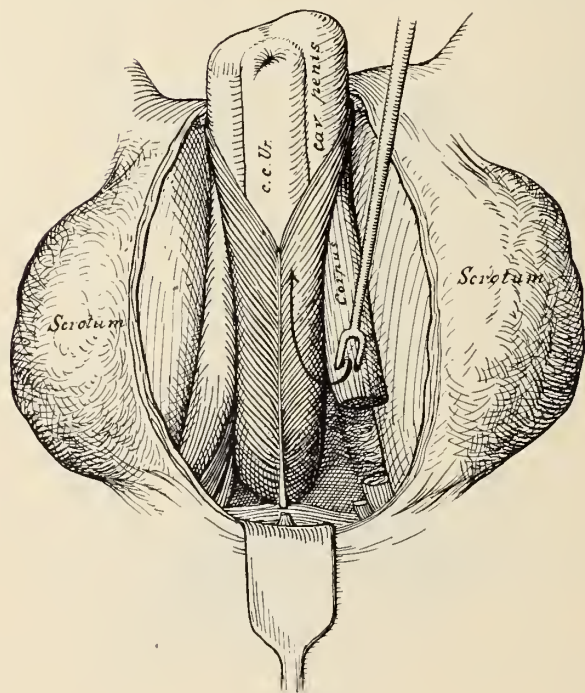
FIG. 4

its insertion at the pubic bone, was completely mobilized, and rotated by 180 degrees (Figures 4 and 5). It was then placed behind the corpus cavernosum urethrae, and fixed in this position by deep sutures. This resulted in an elongation by another five centimeters.

The body of the penis thus obtained had now to be surrounded with new skin by means of a complicated plastic operation. Figure 3 shows the lines of incision. The new skin was taken partly from the skin of the scrotum, and partly from that of the mons Veneris.

Figure 7 depicts the conditions as they presented themselves immediately following the first operation. A rubber catheter inserted in the
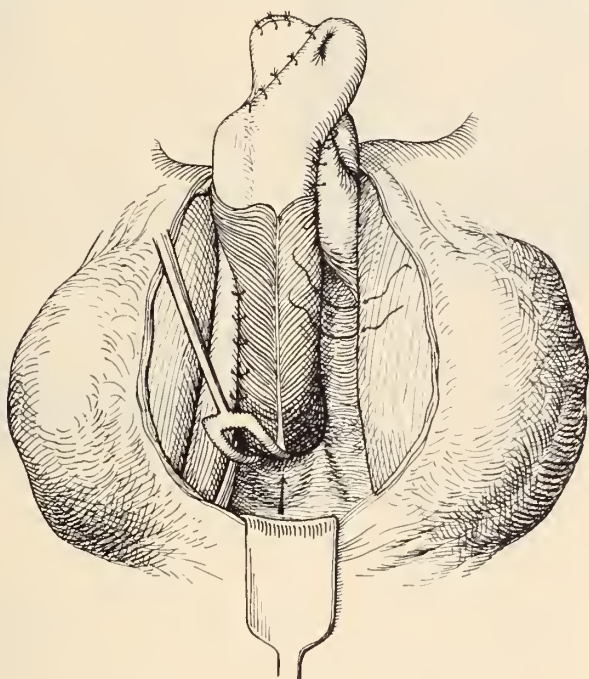
Fig. 5

urinary bladder also served as an extension splint, since the newly gained end of the penis could be forcibly stretched by silk sutures.

The postoperative treatment required many months. The following difficulties arose. Underneath the penis, a very edematous skin fold formed (Figure 8) which pulled the penis toward the perineum and which interfered with erection. Simple cutting of this skin fold and suturing in a longitudinal direction sufficed to remove this obstacle. Then another annoying disturbance grew out of the hairiness of the skin flap taken from the mons Veneris. It compelled the patient to shave the area regularly. I was able to remedy this condition by another operative measure. I laid a subcutaneous sharp incision through the whole length of the hairy skin
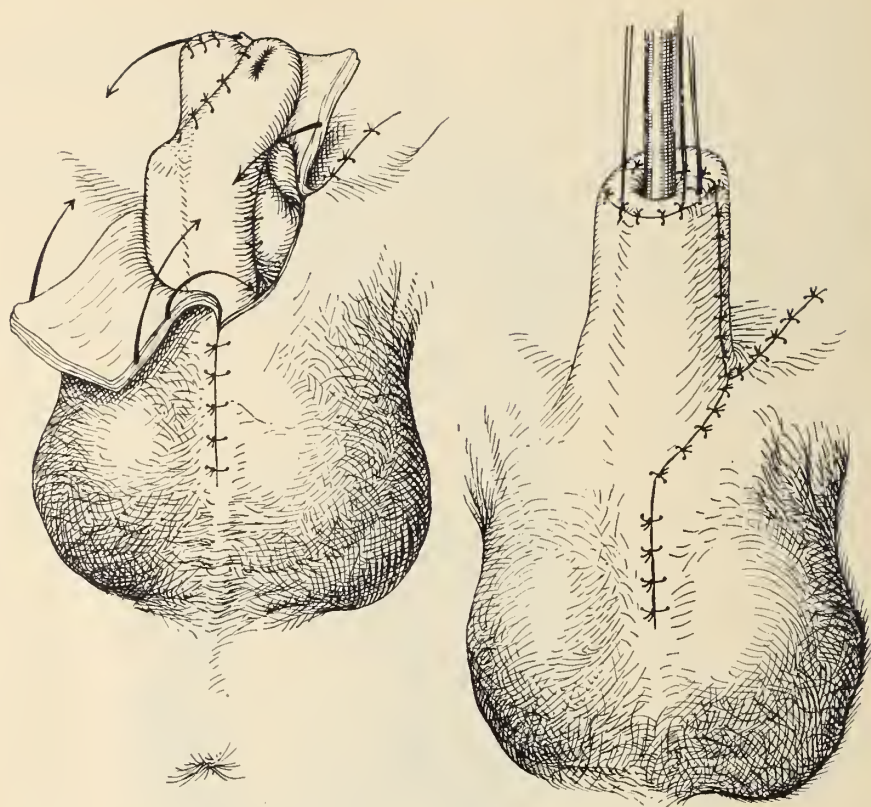
FIGS. 6 & 7
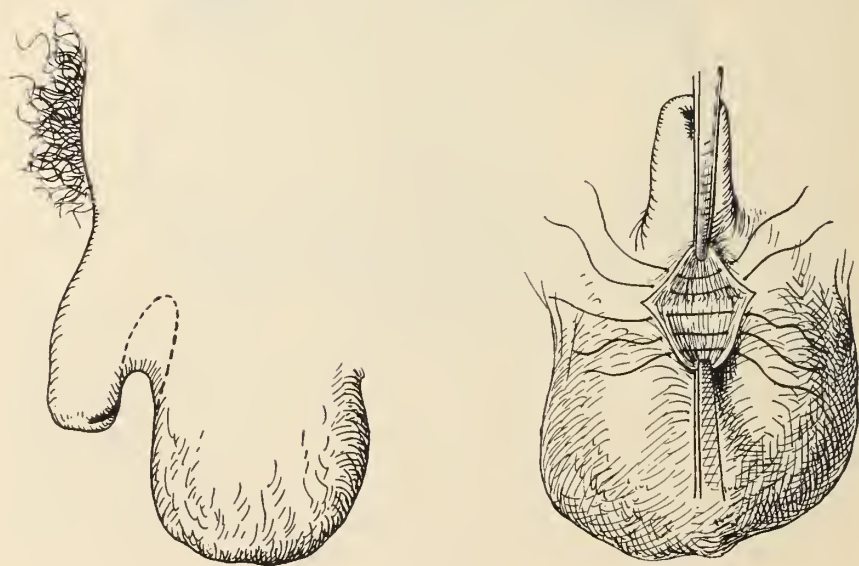
FIG. 8

flap, parallel to its surface. Then, finally, the newly formed penis was covered with completely smooth hairless skin. There remained a good sized skin defect to the left of the newly created penis, because the skin became in part necrotic, as a result of the strong pulling of the sutures. This defect was healed completely by a Thiersch skin graft.

An apronlike edema of the penile skin became one of the most disturbing factors in the postoperative treatment. This edema, during the first postoperative weeks transformed the penis into a shapeless mass. Constant compression of the penile skin with a circular caoutchouc plaster proved very successful in remedying this chronic elephantiasis. The patient applied this plaster every day himself and replaced it every time he took a bath.

One year after all the operative procedures had been complete the patient presented himself to me once more and expressed his great satisfaction over the result of the plastic operation. When erected, the penis measures between ten and twelve centimeters. Cohabitation is possible and is satisfying. The edema has almost completely disappeared and no growth of hair has returned.

THE TREATMENT OF BILATERAL LITHIASIS

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The aim of the operative treatment of unilateral lithiasis is to remove the obstructing calculus, and to enable the affected kidney to resume its excretory function. This involves the cure of infection when present. If it is thought that the kidney cannot recover, nephrectomy is indicated, and it is much safer for the patient to have a disorganised and severely infected kidney removed than to run the chance of having the infection spread to the healthy side after a conservative operation. Nephrectomy is rarely indicated when the calculous kidney is not infected, but it has very definite indications when there is an infection localised to the stone-bearing side.

In dealing with cases of bilateral lithiasis, one finds that a bilateral infection is the rule. Out of thirty-two recent cases, eight were uninfected, one had a unilateral infection, while in twenty-three both kidneys were definitely and often severely infected. Under such conditions, one is naturally inclined to assume that the treatment should be entirely conservative, and that any kidney that has even the slightest excretory value should be carefully preserved. This has been the teaching in the past, but of recent years two factors must also be considered. The first is the great improvement in our methods of dealing with urinary infections, and the second is the principle of renal counterbalance, so ably enunciated by Hinman. It seems to be advisable, therefore, to reconsider the indications for operation, especially with regard to nephrectomy, in the light of these advances.

Classification. Cases of bilateral stone may be divided into four groups. (1) Cases in which the calculi are due to a special diathesis, such as cystine stones. (2) Cases of uninfected calculi. (3) Cases of infected calculi. (4) Cases complicated by anuria.

CYSTINE CALCULI

These stones have a great tendency to be bilateral. In fact, calculi were present in both kidneys in every case I have seen. There is a great tendency for the stones to recur after operation, and for this reason some surgeons have advocated that no operation should be performed. This, however, is an unduly pessimistic line of action. On the other hand, these stones have a smooth surface, and slip easily down the ureter. I have seen one patient who passed over one hundred of them in four years, some from

the right and some from the left kidney. He stated that towards the end of this period he had often more pain and difficulty in eliminating them through the urethra than he had when they were coming down the ureter.

Cystinuria is a defect in the protein metabolism and is therefore incurable. One can, however, do much to prevent stone-formation by medical and dietetic treatment. The patient should be put on a low protein diet, in order to diminish as far as possible the source of the cystine. He should also be given large doses of alkali (about 120 grains of sodium bicarbonate a day) in order to keep the urine permanently alkaline. Cystine crystals are insoluble in an acid, but are freely soluble in an alkaline medium. This treatment will retard, if it does not prevent, stone-formation, but it is not easy to keep a patient permanently on a strict diet, and stones form rapidly if the treatment is interrupted.

If the condition has been undiagnosed, or untreated, it is common to find large stones which have become moulded to the shape of the renal pelvis, together with great numbers of smaller stones in the calyces. The kidney seems to tolerate great masses of cystine calculi very well, and the patient suffers remarkably little pain. A uroselectan pyelogram, however, usually shows that the calyces are dilated, and the renal substance is slowly destroyed by the back-pressure. In such cases operation is indicated in order to save the kidneys.

If the excretory function of the two kidneys is approximately the same, it does not matter which is explored first. The only important consideration is that the second should be freed of its calculi as soon as possible after the first. When the obstructing calculi are small, and entirely confined to the renal pelvis, there is no risk in doing a bilateral pyelotomy in one sitting, but a double operation should not be advised when stones are present in the calyces as well. My reason for making this statement is that I do not think it advisable to perform a double nephrotomy in one sitting. When the function of one kidney is distinctly better than that of the other, one should operate on the more damaged kidney first. It will recover a great part of its function once the obstruction is relieved, and one can safely operate on the other side as soon as the first kidney gives a good response to the tests of the renal function.

These considerations are based on the principle of renal counterbalance. Cystine calculi rarely become infected, so one may assume that the urine derived from both kidneys is sterile. When the function of both sides is approximately the same, this balance is not upset by a bilateral operation performed in one sitting, or by a two-stage operation, provided the interval does not exceed a fortnight. If a longer interval is allowed to elapse between the operations, the first kidney will hypertrophy, and take over the greater part of the total excretion. There will then be no work left for the second. It will have no stimulus to recover, and will either atrophy, or else only preserve a small portion of its excretory activity. A long delay

between the two operations may easily leave the patient with a single functioning kidney, and is therefore similar in its ultimate effects to a nephrectomy.

When the function of one kidney is worse than that of the other, I advise operating on the more damaged side first, and leaving a considerable interval (six weeks to two months) before exploring the second. The function of the first kidney will improve during the interval, and after the second operation the patient will probably have two useful kidneys.

BILATERAL UNINFECTED CALCULI

Cases of bilateral lithiasis associated with sterile urine are comparatively rare. In the personal series mentioned above, eight out of thirty-two patients were free from infection. Two of them had cystine stones, so that six, or less than one fifth of the total, had uninfected calculi of the ordinary type. In these cases the stones were usually composed of calcium oxalate. They differ from cases of cystine lithiasis in that the calculi are usually small, and that they are frequently impacted in the ureter. Cystine calculi rarely become lodged for any length of time in the ureter, though a few cases of this condition have been reported from time to time.

This group comprises the most satisfactory cases of bilateral stone with which the surgeon has to deal. The stones are generally small, recurrence is not common, and the renal function is usually well preserved on both sides. It is rare to find severe renal damage, such as marked hydronephrosis, occurring with uninfected calculi. At the same time, there is always a risk of anuria developing, though this complication is, in my opinion, more common when infection is present. Nephritis may arise if the case has been neglected, and the calculi allowed to remain indefinitely. I have seen a fatal nephritis in a woman who was known to have bilateral renal calculi for nine years. There was no excuse for inaction in this case, as the patient had marked symptoms both from the lithiasis and the nephritis. As a matter of fact, she was told that no operation was necessary because the stones were not increasing in size. This, however, is an indication that the kidneys are failing, and that operation is urgently necessary to save them.

In these cases, where the urine is sterile, it is rare to meet with more than one stone on either side. The presence of multiple calculi usually means that the kidney is grossly dilated, and has in consequence a poor functional value. One may find that a stone is lodged in each renal pelvis, or in each ureter, or else that there is a pelvic calculus on one side with a ureteric one on the other. As a general rule operation should be performed without delay, unless it is certain that the patient can pass the stones easily. If there is any doubt on this point, it is safer to operate than to allow the patient to run the risk of anuria.

If both calculi lie in the ureters, they may be removed at one sitting. It is easy to explore the pelvic portions of both ureters through a single midline incision. If, however, they lie above the brim of the pelvis, two incisions will be necessary, but this does not materially increase the severity of the operation. If both calculi lie in the renal pelvis, one may also operate on both sides at the same time, provided one is certain that they can be removed by pyelotomy. In this case, the patient is placed on his face, the surgeon operates on one side, while his assistant exposes the opposite kidney. A two-stage operation is indicated when it is thought probable that a nephrotomy will be necessary, but this contingency can usually be foretold from an examination of the pyelograms. It is very seldom that a bilateral nephrotomy will be necessary, but, if it is thought probable that one stone can be removed by pyelotomy, it should be dealt with first. The more serious operation (nephrotomy) can be performed a fortnight later.

If there is a stone in one renal pelvis, associated with another in the opposite ureter, I usually prefer to remove the ureteric calculus first, and to deal with the kidney a fortnight later. My reason for this method is that a ureteric calculus generally gives rise to a greater degree of obstruction than one in the renal pelvis, and should therefore be removed as soon as possible. These cases are generally unsuitable for a simultaneous bilateral operation, as it is necessary to change the patient's position when one stone has been removed, and the whole procedure is prolonged unduly.

When one kidney is severely damaged, and its excretory value is considerably less than that of its fellow, one should always operate on the damaged organ first. It will probably recover a great part of its function if given sufficient time to do so. For this reason the patient should be carefully watched during the interval between the two operations, and as soon as the function of the damaged organ approximates to that of its fellow, the stone should be removed from the latter. In this way only will the normal balance between the two kidneys be restored. Complete destruction of a kidney caused by an uninfected stone is a rare occurrence. I have only seen one case of it, and that was in a patient suffering from unilateral lithiasis. If it is met with in a case of bilateral stone, one should naturally operate on the sole functioning kidney first, and at a later date remove the useless organ. It is, however, always difficult to determine whether the loss of function is only temporary or permanent. When there is any evidence that the better of the two kidneys has already become hypertrophied, as is usually the case, its fellow can never recover, and had better be removed. It is only when the function of both sides is below normal that there is a possibility of restoring some function in the more damaged.

Large bilateral calculi are often present in cases of hyperparathyroidism. Fortunately this rare condition can be diagnosed by an estimation of the

blood calcium and phosphorus. Unless the renal condition is urgent, it is best to correct the parathyroid excess first, and then to deal with the calculi according to the lines laid down in the preceding paragraphs. The stones are phosphatic, and grow rapidly. They have a great tendency to recur, unless the primary condition is relieved. In this respect they resemble cystine calculi. They originate in uninfected urine, but their presence naturally paves the way for infection.

BILATERAL INFECTED LITHIASIS

This is not only the most common, but also the most dangerous group of cases. The kidneys are damaged both by the mechanical obstruction caused by the stone, and by the inflammatory changes brought about by the presence of micro-organisms. The aim of the surgeon is twofold. He must remove the calculi, and at the same time cure the infection. If the latter persists, a recurrence of the lithiasis is almost certain.

The infection may be primary or secondary, as far as the urinary organs are concerned. In the former condition, the kidneys are infected before the stones form, in the latter an aseptic calculus or calculi subsequently become infected. In many instances it is difficult to ascertain to which class a patient belongs, as the onset of infection is often insidious and may not be noticed by the patient. I think, however, that in most instances the infection is primary, and that it is responsible for the stone formation.

The infection may be either haematogenous or ascending. A haematogenous infection may start as an acute pyelitis which does not clear up completely, but becomes chronic and symptomless. The acute stage may be transient and soon forgotten by the patient, who simply complains that his water is "thick" or "cloudy", and can give no information as to the duration of this symptom. When the urinary infection follows a severe general illness, one has no difficulty in determining its duration. Septic compound fractures are frequently associated with lithiasis, which has a marked tendency to be bilateral. In such cases there are three factors, all of which predispose to stone-formation. The first is sepsis, the second prolonged immobilisation, and the third is the absorption of calcium from the skeleton. The bone becomes rarified in the region of the fracture, and in addition immobilisation is always accompanied by absorption of calcium from the whole of the skeleton. There is no reservoir in which the lime can be stored in the body, so it is eliminated in the urine as fast as it is absorbed from the bones. During the European war a large number of these cases were observed, and an interesting series was reported by Paul.

Ascending infections are undoubtedly more often the cause of bilateral lithiasis than we formerly thought. Hellström has pointed out that a chronic staphylococcal infection of the kidneys is a frequent cause of stone-formation. He considers that in many cases it originates from a

post-gonorrhoeal involvement of the prostate and seminal vesicles, and
I have seen cases which conform exactly with this hypothesis.   It is well
known that bilateral stone is exceedingly common in cases of fracture-
dislocation of the spine, when the infection undoubtedly originates from
the bladder.   Children suffering from spinal caries, hip joint disease, and
similar conditions often show radiographic shadows resembling those pro-
duced by renal calculi.   These shadows grow very quickly, and rapidly
involve the calyces, so that they resemble a pyelogram.   They are prob-
ably due to masses of sand rather than to true calculi, as in many instances
they disappear when the child has recovered sufficiently to run about.   It
has also been found that this condition can largely be prevented by giving
large quantities of fluid, and also by nursing the patients on specially de-
signed frames which can be tilted in any direction, so as to allow frequent
changes of position.

When discussing the operative treatment of bilateral infected lithiasis,
one must consider separately (1) cases where the renal function is ap-
proximately the same on both sides, and (2) cases where the value of one
kidney is much greater than the other.

In the first group one occasionally meets with cases where the total
renal function is so much impaired that no operation is feasible.   Uro-
selectan pyelograms are of great use in deciding this point.   I have seen
cases where there was no visible excretion of this drug in radiograms taken
up to forty-eight hours after injection.   At the same time there is marked
nitrogen retention, and the response to other tests (P.S.P. and urea con-
centration) is equally bad.   I am, however, prepared to operate on any
patient who excretes sufficient uroselectan to enable one to visualise the
pelvo-calyx systems, even though there may be a marked delay in excre-
tion.   In these border-line cases, a bilateral nephrostomy is of great use,
as it relieves both the obstruction and the infection, and enables the kid-
neys to recover a portion of their lost function.   The stones may be re-
moved later, when the patient's condition has improved.

If the renal efficiency is fair, the treatment depends on the size and posi-
tion of the calculi.   Pelvic stones without prolongations extending into
the calyces should always be removed.   I think it safer in the presence of
infection to operate in two stages, as the reaction may be severe.   How-
ever, the interval between the two stages should be as short as possible.
The most difficult cases are those in which the stones form casts of the
pelvo-calyx systems on both sides.   Patients with bilateral "stag horn"
calculi usually have a fair renal function, but the infection is always severe
and difficult to treat.   The reaction of the urine is usually strongly alka-
line, and it is impossible to modify it by giving acidifiers by mouth.   The
infecting organism is often the Bacillus Proteus, which is the most potent
of the urea-splitting organisms.   So long as it is present one cannot hope
to render the urine acid, and the urinary antiseptics which act only in an

acid medium are useless. It is in such cases that one hopes for better results from the administration of prontosil or sulfanilamide. These drugs have a bactericidal action in alkaline urine, but they are still on trial, and it is too early to speak of their therapeutic value. Before deciding on operation in cases of bilateral stag-horn calculi, it is most important to ascertain if the stones are giving rise to retention within the kidney. This can be determined most easily by means of an intravenous pyelogram. If there is retention, such a pyelogram will reveal the presence of a considerable amount of fluid surrounding the calyceal portions of the calculus. The calyces are thus shown to be much larger than the portions of the stone lying within them, and the latter can be extracted without doing much damage to the renal tissue. On the other hand, if there is little or no retention, the uroselectan shadow merely outlines that of the stone. Each calyceal projection of the calculus is then usually club shaped, with a narrow neck, and an expanded proximal end. It fits the calyx tightly, and cannot be extracted without doing great damage to the surrounding renal tissue. In the former case I consider that operation is feasible, but in the latter I feel that it is in the best interest of the patient not to attempt to remove the stones. These patients often live for many years with enormous stone masses in both kidneys, but the renal efficiency slowly diminishes, and they ultimately die from uraemia.

When the excretory value of one kidney is much better than that of the other, it generally means that the lithiasis was at first unilateral and confined to the more damaged organ, but that later on the better kidney became infected and stones developed in it also. This is a common occurrence, and has a distinct bearing on the question of treatment. When the lithiasis was confined to one side, every diminution in the excretory function of the affected kidney was followed by a corresponding degree of hypertrophy of the healthy organ. In this way the difference between the excretory values of the two kidneys becomes progressively greater, until the healthy organ takes on the total function of waste elimination. If a calculus now forms in it, the hypertrophy does not diminish, although the response to the renal function tests may be temporarily lowered. One then has to deal with a large stone in an almost functionless organ associated with a small calculus in a hypertrophied kidney. The operative indications are, therefore, a pyelotomy on the side last affected, followed by removal of the severely damaged kidney. It is not always easy to perform a pyelotomy when the kidney is hypertrophied, as the renal pelvis does not enlarge with the increased size of the kidney. It becomes hidden in the renal sinus, and good retraction is necessary in order to expose it.

Of course, after operation the residual infection must be combated by urinary antiseptics.

CALCULOUS ANURIA

Only those cases of calculous anuria in which both kidneys are obstructed come within the scope of this paper. The calculi may lie in both renal pelves, in the renal pelvis on one side and in the opposite ureter, or in both ureters. The last is by far the most common situation. It is also usual to find the obstructing stones in the upper ureter.

Complete urinary obstruction is followed by an early and rapid rise in the amount of the blood urea, and after a delay of four or five days by the onset of uraemia. It is always fatal unless the obstruction is relieved, or the stone becomes disimpacted.

The first step in the treatment is to pass catheters up both ureters. If they can be insinuated above the stones, there will be a brisk elimination of urine through them. They are left in situ, and the patient's kidneys are stimulated by large quantities of fluids. The blood urea rapidly falls, and the patient's condition improves. By this means one gains time to investigate the position of the stones etc., and can perform a set operation under good conditions. It is important that the catheters should not be removed until the commencement of the operation, as it is extremely dangerous to allow the obstruction to recur.

If one fails to pass a catheter above the obstruction, or if it does not drain satisfactorily, one should cut down immediately on the kidney. Time should not be wasted looking for the calculus, but the operation should be considered as an emergency procedure to secure drainage. I prefer to put a self-retaining tube into the renal pelvis, but many surgeons insert a tube through the renal parenchyma until its end lies in the pelvis. When the patient has fully recovered from the effects of the anuria, steps should be taken to remove the calculi. If one considers that the kidney first exposed is incapable of excreting urine, the patient must be turned over and the opposite kidney explored. In this case both should be drained, but in most cases unilateral drainage is sufficient. If the patient passes no urine per urethram after one kidney has been drained, it means that the undrained kidney is still obstructed. The surgeon should then remove the calculus from the undrained side as soon as the patient's condition allows.

The great advantage of ureteric catheterisation is that it enables the surgeon to avoid an emergency operation, and puts him in a position to remove the obstructing calculi under safe conditions.

INFECTED BRONCHOGENIC CYSTS IN THE LUNGS, WITH SIMULATION OF EMPYEMA

EINAR KEY

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It is well known that occasionally an acute septic empyema does not heal after thoracotomy and drainage but instead passes over into a chronic stage. In other instances there occurs apparent healing but recurrence follows. Both events require new, often repeated operations and it is not infrequently very difficult to attain permanent healing. In order to prevent the development of a chronic or recurrent empyema, it is necessary to ascertain as accurately as possible the extent and position of the acute empyema and to follow the postoperative course of healing. In this connection repeated röntgen examination is of great assistance.

My object here is to draw attention to the fact that large infected pulmonary cysts may be confused with empyema and be treated as such. Naturally it is impossible in these cases to obtain a cure by thoracotomy and drainage. Other more drastic interference is necessary. It is therefore of great importance that these cases are diagnosed correctly and early enough.

Over a relatively short period I had referred to me no less than three such cases, all diagnosed as chronic empyema, which I was supposed to attempt to cure by plastic operation. I shall now give a brief account of my experience with these cases.

Case I. Boy 10 years of age. Following measles, acute onset with stitch in left side and rising temperature. Admitted early in 1931 to local hospital under diagnosis of acute empyema. Immediate thoracotomy with removal of 200 c.c. of pus. No healing. Reoperated twice in 1931. Notes from last operation: "A finger inserted in the pleural cavity palpated, especially at its borders, a network of fibrous adhesions which were then broken down by blunt dissection and scissors. Anteriorly there was a large tough adhesion which, when released, allowed entrance into another large cavity. The operation had to be stopped on account of profuse hemorrhage." The cavity did not heal and has been draining through a tube ever since. The patient was referred to me for radical operation and was admitted to Maria Hospital 11/4/1935. During 1935 his general condition had improved. The röntgen examination showed a large cavity in the lower lobe of the left lung (Figs. 1 and 2). Injection of iodipin into the cavity revealed the presence of an additional system of
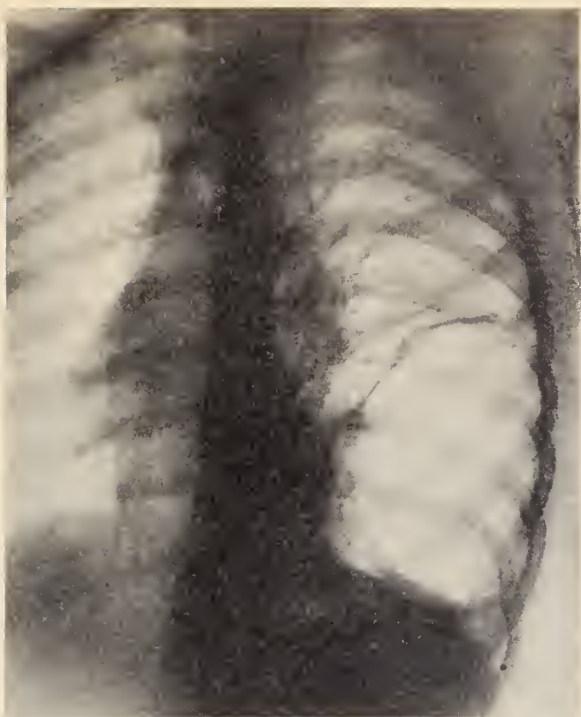
FIG. 1. Case 1. Röntgenogram showing a large cavity in the lower lobe of the left lung

FIG. 2. Case 1. Röntgenogram, lateral view

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small cavities medially and basally (Fig. 3). The picture was suggestive
of a congenital cyst and the existence of only an insignificant pleural thick-
ness on the röntgen films was also against a diagnosis of chronic empyema.

With the intention of doing a lobectomy, operation was undertaken
11/7/1935 and the eighth, ninth and tenth ribs were resected. The
lower lobe of the lung contained a large hole. Adhesions were broken
down, which fixed the lower lobe to the diaphragm, chest wall and peri-
cardium. On the release of the pericardium, the free pleural cavity was
opened but, as the patient began to show signs of exhaustion, it seemed

FIG. 3. Case 1. Röntgenogram showing additional system of small cavities
medially and basally, revealed after injection of iodipin

safest to stop the operation. A tampon was inserted around the freed
portion of the pulmonary lobe. The patient was allowed to go home for
Xmas and on his return a new operation was undertaken 2/14/1936 and
the sixth and seventh ribs had to be resected. The remaining adhesions
which tied down the lower lobe were released and the lobe extirpated.
Tamponage. The patient was discharged 3/16 to his local hospital with a
small bronchial fistula which later healed and he is now well and healthy
(Fig. 4).

A number of wide bronchial lumina opened into the cavity in the lower
lobe of the lung. The wall of the cavity consisted of fibrous connective

tissue containing inflammatory cells and was lined by multiple layered cylindrical epithelium. Beside the large cyst were numerous smaller ones. "The histological picture suggests a tissue malformation arising from the bronchial system" (Wahlgren).

It seems to me that this from the beginning was one large infected bronchogenic cyst with adjacent smaller cysts, the whole being diagnosed as an empyema and treated as such. If one now scrutinizes the röntgen films

Fig. 4. Case 1. Photograph showing completely healed scar

taken before the first empyema operation in 1931, there is a cavity in the lower pulmonary lobe (Fig. 5). This picture could have suggested the correct diagnosis from the beginning.

Case 2. Boy 13 years of age. Acute onset 5/30/1928 with cough and marked fever. A week later thick pus was removed by thoracentesis. After one more tapping with removal of pus, thoracotomy and drainage was done in the local hospital. Repeated subsequent operations did not lead to permanent healing. The patient was referred to me for radical operation and was admitted to Maria Hospital 1/17/1937.

The röntgen examination revealed a large cavity in the right lower pulmonary lobe (Fig. 6). The pictures seemed to me suggestive of an infected pulmonary cyst. A comparison with the pictures from 1934 (Fig. 7) and 1935 showed that the cavity had remained relatively unaltered during the entire period. In order to convince myself whether it was a question of an infected cyst or an empyema, the cavity was opened widely at operation 1/20. It turned out that the cavity was situated within the lower pulmonary lobe and that several bronchi opened into it. The lower lobe
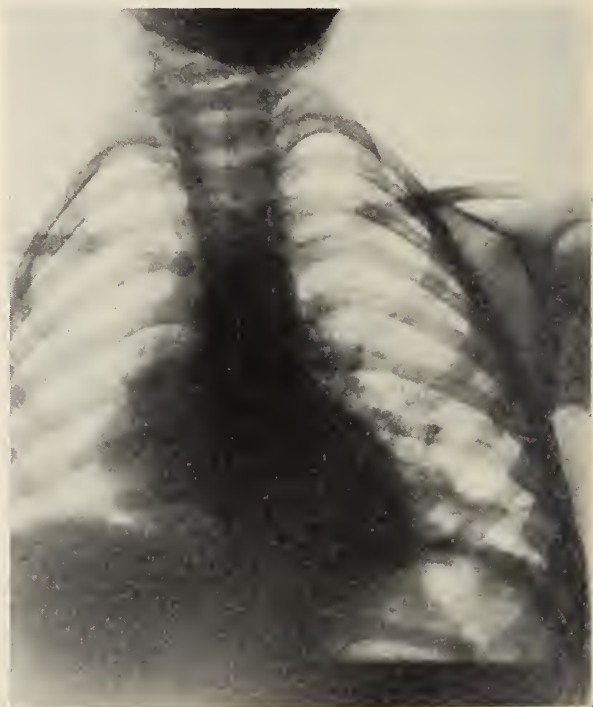
FIG. 5. Case 1. Röntgenogram taken before the first empyema operation in 1931 showing a cavity in the lower lobe

was adherent to the adjacent tissues so some of the adhesions to the diaphragm had to be broken down. On account of the tough adhesions, it was necessary to do the operation at two sittings. The pulmonary tissue was rather easily released from the diaphragm. At the second seance a severe venous hemorrhage arose when releasing the lung medially and the operation had to be broken off. The rest of the adhesions were released 3/22 and lobectomy done. The border toward the lung was difficult to find and only an extremely thin layer of lower lobe tissue remained. Tamponage. The patient was discharged to his local hospital 7/16 not fully healed but with a small bronchial fistula. He is to return for closure of the fistula, if that turns out to be necessary.

FIG. 6. Case 2. Röntgenogram taken in 1937

FIG. 7. Case 2. Röntgenogram taken in 1934

The cyst wall was composed of collagenous relatively acellular connective tissue in which lay numerous small bronchus-like structures. The lumen of the main cyst was lined chiefly by multiple layered cylindrical respiratory epithelium with here and there squamous non-cornified epithelium. "Bronchial cyst with inflammatory lesions" (Wahlgren).

Case 3. Boy 10 years of age. Onset with high fever and large quantity of sputum. Admitted to local hospital beginning of June 1934. Thoracentesis 6/4 revealed thick greenish-yellow pus. On tapping some days later the syringe needle first entered the free pleural cavity and then when pushed deeper reached thick non-odorous pus. Thoracotomy 6/16. The pleural cavity was obliterated through loose adhesions. The lung surface medially felt like a firm wall. When this was perforated by blunt

Fig. 8. Case 3. Röntgenogram showing a cavity situated inferiorly and extending up as high as the hilus

dissection large amounts of pus and air escaped. Drainage. Discharged November 1934. The wound never healed and he was repeatedly readmitted to local hospitals and operated upon.

He was then referred to me for radical operation under the diagnosis of pleural empyema on the left side with a fistula following pulmonary abscess. Admission to Maria Hospital 3/19/1937. Röntgen examination and injection of iodipin through the fistula revealed a cavity situated inferiorly rather far posteriorly and extending up as high as the hilus. Medial to this cavity was a bronchiectatic area as large as a hazel nut (Fig. 8). I performed thoracotomy with resection of the fourth and fifth ribs 3/23. There was no empyema but instead the cavity was entirely within the lower lobe. It extended up rather far and seemed to be quite

narrow superiorly. As it seemed to me rather risky to do a lobectomy in the presence of firm adhesions, I decided to try to destroy the epithelial lining of the cavity by means of etching so that the walls could fuse after a plastic operation. The inner surface of the cavity was therefore painted with 20 per cent silver nitrate, during which procedure the bronchial lumina opening into the cavity were held closed by compresses. The cavity was painted on two further occasions with Zenker's solution and an aseptic thoracoplasty with resection of portions of the third and sixth ribs was done. This, however, did not produce the desired result, so I felt bound to try a lobectomy. The inferior lobe was firmly adherent to the neighborhood. During the release of the adhesions the patient reacted badly so that the operation had to be done in three sittings 5/4, 5/21 and 6/1. At the last operation when after great difficulties the lobe was practically freed, the patient suddenly took a turn for the worse and died of air emboli.

The inner surface of the cavity was lined by a single layer of cubical epithelium supported by a rather broad zone of collagenous connective tissue profusely infiltrated with inflammatory cells and containing a few smooth muscle cells. The adjacent tissues showed a few small areas of bronchiectasis. "The histological picture suggests a bronchogenic cyst with inflammatory changes" (Wahlgren).

The patient was at first treated in his local hospital under the diagnosis of lung abscess and empyema. When repeated operations did not result in a cure, he was referred to me under the diagnosis of empyema with post-operative fistula and pulmonary abscess. Operation at Maria Hospital showed that there was no empyema but that the fistula went directly into a large cavity in the lower lobe of the lung.

Bronchiectasis and bronchiectatic cavities are not unusual and not infrequently lead to lobectomy. It would seem unusual, however, that a bronchogenic cyst would be large enough to be confused with empyema. If one knows about these cysts and remembers to think of them, the correct diagnosis can usually be arrived at.

Bronchogenic infected cysts cannot, like acute septic empyema, be cured by thoracotomy and drainage. Instead it is necessary to do lobectomy. It is of great importance that the correct diagnosis be arrived at in time so that these patients are not incorrectly treated over long periods for empyema. It is also essential to make an early diagnosis so that the lobectomy can be done before the adhesions have become too tough. Such adhesions hamper the operation greatly and increase its danger. I shall not discuss here the technique of lobectomy, but only point out that in general it is preferable to do the operation in one rather than several seances and to use a tourniquet around the hilus. Often, however, on account of tough adhesions, it may be difficult to free the lobe and several seances may be necessary. When a tourniquet cannot be placed around

the hilus early, and the adhesions must instead be broken down bit by
bit, the danger of the operation is greatly increased.   Lung tissue is easily
torn and there is a great opportunity for air embolism.   One should try
to place a tourniquet around the hilus as early as possible in order to pre-
vent the formation of air emboli.

On the basis of my experience with the third case, I consider it inadvis-
able to try to free the lung lobe bit by bit from tough adhesions extending
from the opening in the thoracic wall up to the hilus, for these adhesions
around the thoracotomy opening are the most fibrous.   Instead, possibly
through a special incision in the chest wall, one should first try to isolate
the hilus and place a ligature or tourniquet around it and subsequently free
the pulmonary lobe, if necessary, at a later sitting.   I have used this
procedure in a recent case.

In her local hospital a girl five years of age had had a thoracotomy for a
lung abscess in the right lower lobe when she was one year old.   After
several more thoracotomies and rib resections she was referred to me for
radical operation and was admitted to Maria Hospital 8/10/1937.   She had
then a wide open cavity in the right lower lobe.   Several bronchi opened
into the floor of this cavity.   Röntgen examination and injection of a
contrast medium revealed several smaller cavities in the neighborhood of
the large one in the lower lobe.   In this case I first exposed the hilus and
placed a silk ligature around it.   As her general condition became worse
during this procedure, I dared not do a lobectomy at the same sitting.
Eight days later I performed a lobectomy and the subsequent course was
normal.

URINARY OBSTRUCTION IN CHILDREN

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Diseases of the genito-urinary tract in infants and children are sufficiently common to rate them among the important lesions in early life. Repeated studies in children have revealed that they are subject to practically the same urological diseases as adults. However, the most common lesions found in the urinary tract of the young are obstructive in type, and the great majority of them result from anomalous development. When one realizes that the incidence of congenital anomalies in the genito-urinary tract is higher than in any other system of the body, it can be appreciated why the greatest field of urology today lies in the early diagnosis and treatment of these abnormalities.

The study of urological disease in children is not new, yet the importance of a complete urological investigation in the young has not been fully appreciated by the medical profession in general until quite recently. We have failed consistently to realize the gravity of persistent urinary complaints and findings. In the past few years there has been a beneficial change. Internists and pediatricians have been very willing to coöperate with the urologists, with the result that today many more children are being investigated urologically than ever before. Moreover, all children's hospitals of repute have come to realize the importance of genito-urinary diseases in children, and have established urological services. It is to be hoped that this cooperation will be even more striking in the future, with beneficial results both to the doctors and the young patients.

Any obstructive lesion in the genito-urinary tract is of prime importance because of the back pressure and destructive changes that it eventually produces on the renal parenchyma. It is also an important etiological factor in causing urinary stasis and infection. If the obstructive lesion is not removed the destructive process goes on until the kidney or kidneys are destroyed. The importance of recognizing early such obstructing lesions is apparent. For the sake of emphasis we wish to discuss briefly two specimens that were found in young children.

The first one was removed at operation (Fig. 1). It shows a destroyed kidney with a large dilated ureter. There are three definite obstructive lesions present. One is at the ureteropelvic junction, another at the junction of the middle and lower thirds of the ureter, and a third (not shown on the photograph) near the ureteral orifice. We feel justified

in saying that if the obstructions had been recognized at an early date, proper procedures could have been carried out, thus preventing the complete destruction of both kidney and ureter.

The second specimen was found at autopsy (Fig. 2). The child, male, age 9 years, was admitted to the hospital in uraemia. A diagnosis of bilateral pyonephrosis and pyo-ureter was made. He died shortly after.
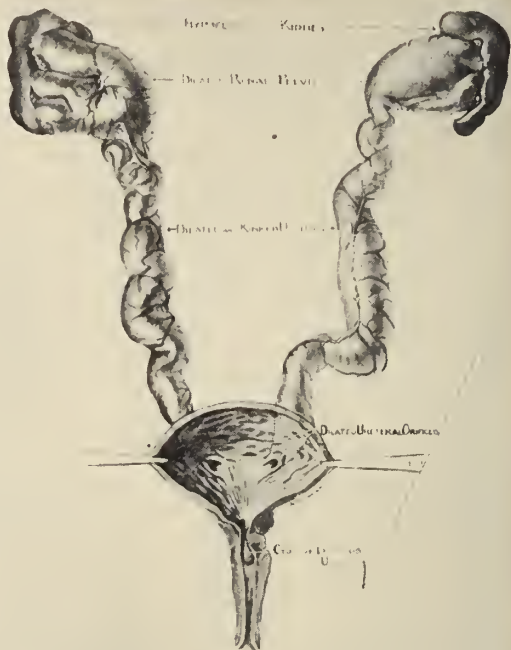
FIG. 1.   FIG. 2

FIG. 1. Photograph showing a destroyed kidney and a large dilated ureter removed from a young child. There are two definite obstructive lesions shown, one is at the ureteropelvic junction and the other at the junction of the middle and lower thirds of the ureter. There was a third obstruction near the ureteral orifice (not shown in this photograph).

FIG. 2. Photograph of drawing of a specimen removed at autopsy from a male child, aged nine years. Note the large dilated renal pelves and ureters; also the trabeculated bladder, and the presence of a cyst in the posterior urethra.

The post mortem examination revealed completely destroyed kidneys, large dilated ureters, trabeculations and diverticula of the bladder, and finally a cyst in the posterior urethra. Apparently this cyst caused an obstruction which ultimately destroyed the urinary tract. This case too stresses the need for early recognition of urinary obstruction. It is reasonable to assume that the urinary tract might have been saved from

Fig. 3. Photograph of a specimen removed from a young child, illustrating the presence of several obstructive lesions in the same organ. *Note* (1) the narrowing at the ureteropelvic junction, (2) the presence of multiple valve-like projections about the middle third of the ureter and (3) a narrowing of the ureter as it enters the bladder.

complete damage if the child had undergone an urological examination earlier in life.

Campbell in a recent article on urinary obstruction in children emphasized this very point by stating that the greatest field for preventive medicine today lies in the early recognition and treatment of these obstructive lesions in the young. It becomes vitally important therefore for the physician and urologist to coöperate early whenever an obstructive lesion of the urinary tract is considered. It is of interest to emphasize at this time the prevalence of multiple obstructive lesions in the same organ. It is not uncommon to discover at operation or on the autopsy table, two or three varieties of congenital lesions along the course of the one ureter. This possibility must always be borne in mind by the surgeon (Fig. 3).

Urinary obstruction in children may be divided into two groups:
1. Upper urinary tract obstructions
2. Lower urinary tract obstructions.

In the upper urinary tract group the obstruction may be encountered anywhere along the ureter, including the ureteral orifice. The lower urinary tract lesions, on the other hand, include all obstructions occurring anywhere from the external urethral meatus to the bladder neck.

UPPER URINARY TRACT OBSTRUCTIONS

1. *Obstruction Due to Aberrant Vessels.* Although vascular obstruction of the ureter in children is not an uncommon occurrence, yet the condition is frequently unrecognized and rarely diagnosed. The aberrant vessels, which may be arteries, veins, or both, usually cross anteriorly to the ureter. The most common site of these vascular obstructions is in the upper portion of the ureter, although cases have been observed where the vessels transverse the lower portion of the ureter near the bladder. It will be appreciated at this point that not all anomalous vessels that cross the ureter cause urinary obstruction. Several cases of aberrant vessels have been observed at autopsy and on the operating table, without any evidence of hydronephrosis or hydroureter.

There has been considerable controversy regarding the etiological relationship of aberrant vessels and hydronephrosis. It is believed by some that hydronephrosis results from direct compression of the ureter by the vessel; others are of the opinion that there is primarily some renal ptosis which, in turn, causes the aberrant vessel to compress the ureter. Quinby assumes that the pulsation of the aberrant artery against the ureter inhibits peristalsis and so causes stasis.

The pathological picture depends upon the degree of obstruction and the length of time it has been present. In early cases a mild hydronephrosis is found; as the compression becomes more aggravated greater stasis results, until finally infection sets in, and now there is a large infected hydronephrosis. Ultimately the entire kidney is destroyed.

The symptoms of aberrant vessel obstruction are those of hydrone-phrosis with or without infection. A common symptom is pain. This is usually present in one or other loin, and may be dull or colicky in charac-ter. At times the pain is confined entirely to the abdomen. Often the pain is associated with chills, fever, nausea and vomiting. More fre-quently the picture is suggestive of a gastro-enteritis. Recently we observed a case that resembled an acute intussusception. The symp-

Fig. 4. Pyelogram showing a large hydronephrosis on the left side. This was due to an aberrant artery and vein which were firmly adherent to the lower portion of the pelvis.

tomatology is characteristically intermittent. There may be long intervals of months or even years, during which time the patient may be absolutely free of symptoms. On the other hand, attacks may occur very frequently.

When infection sets in symptoms of cystitis appear. There is fre-quency, dysuria, and even haematuria. In late cases a mass may be felt in the loin, and when fever and chills are present severe tenderness may be elicited on palpation. Systemic symptoms may also be present. This, of course, results from long standing urinary infection, and diminished

renal function. The child has anorexia, becomes anaemic and loses weight. If a lesion is present on both sides uraemia may set in, with malaise, vomiting, and even stupor.

There are no signs or symptoms that are pathognomonic of aberrant vessel obstruction. Other forms of urinary obstruction may give the same clinical picture. However a positive diagnosis can be made in

DIAGRAMMATIC DRAWING

LEFT KIDNEY ANTERIOR VIEW

A.
V.

HYDRONEPHROSIS OF PELVIS

ABERRANT VEIN
" ARTERY
FIRMLY ADHERED
TO PELVIS
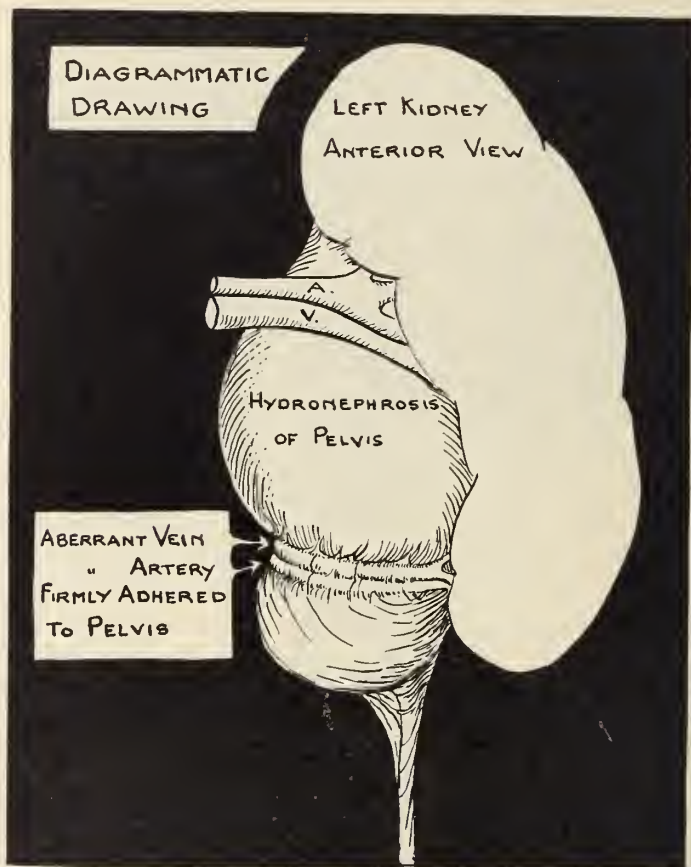
FIG. 5. Diagrammatic drawing illustrating the anatomy of the above case (Fig. 4). *Note* the aberrant vessels crossing the lower portion of the pelvis and being quite adherent to it.

many cases if all available data are studied. Thus the history, physical examination, urinalysis, kidney function tests, and finally cystoscopy with pyelography, are all important in the diagnosis. The pyelogram undoubtedly is the most important single aid. There is usually a hydronephrosis with at times an abrupt transverse ureteral obstruction below it (Figs. 4 and 5). Occasionally the obstructing vessel causes a complete filling defect in the outline of the pyelogram. In extreme cases the pyelographic substance does not pass beyond the obstruction.

The treatment of this lesion is always surgical. Whether the procedure will be radical or conservative will depend, of course, on the condition of the kidney. If the obstruction has been present for a long time and has caused severe renal damage, then a nephrectomy may be necessary. On the other hand, if the kidney has not been irreparably hurt, a plastic operation will be the procedure of choice. The type of operation will depend on the size and position of the vessels. Small arteries may be sacrificed. If the aberrant vessel is too large some form of plastic operation is to be performed. There are several such procedures. Transplantation of the ureter into another portion of the pelvis has been recommended by some investigators. Recently Young described a plastic operation whereby the ureter is not severed. He simply removes a portion of the renal pelvis in front, and another portion behind. In so doing, the renal pelvis and ureter are drawn away from the obstructing vessel, thus eliminating the necessity of severing any of these structures. ·

2. *Obstruction of the Ureter by Fibrous Bands.* This type of ureteral obstruction is also common, and is usually encountered at or near the ureteropelvic junction. The fibrous bands may assume a variety of forms. They may appear as longitudinal sheets extending from the renal pelvis downwards along the course of the ureter, or they may run transversely pulling the pelvis and ureter towards the lower pole of the kidney. Not uncommonly these bands encircle the entire ureter causing a definite and often complete constriction at that point. Several of these are associated with a definite stricture. Whether the latter is the cause or the result of the fibrous bands is debatable. The pathological picture, the clinical history, and the physical findings are identical with those of aberrant vessel obstruction. Even the pyelographic studies may be the same (Fig. 6).

The treatment of this condition is primarily to overcome the obstruction, and operation should be performed before the renal parenchyma is destroyed. In early cases the proper procedure is simply to remove the obstructing fibrous bands. Usually this can be accomplished very readily. In a large hydronephrosis a portion of the renal pelvis may be removed. It must be appreciated that more than one obstructive lesion of the ureter may be present, and the proper procedure in each case is to be carried out. For example there may be a constriction at the ureteropelvic junction, and one or more aberrant vessels crossing the ureter (Fig. 7). Recently we encountered a case with bilateral obstruction at the ureteropelvic junction due to fibrous bands, and also a symmetrical narrowing in the lower third of each ureter due to a heaping up of mucosa. This thickening did not encircle the entire lumen of the ureter, but only its posterior portion, the picture resembling a true valve. Above this point each ureter was markedly dilated; below the narrowing the ureters were of average calibre.

3. *Ureteral Stricture.* This pathological lesion is one of the most

common causes of ureteral obstruction. Campbell in a large series found that 50 per cent of the cases of ureteral blockage were due to strictures. He reported one hundred and one such lesions in 1936. The stricture may occur anywhere along the course of the ureter, but the most common sites are at or near the ureteropelvic junction, and near the ureteral

Fig. 6. Pyelogram showing a large hydronephrosis on the right side. At operation several tight fibrous bands were found at the ureteropelvic junction.

orifice. Bilateral strictures may also occur; Campbell found twenty-three such bilateral lesions in his one hundred and one reported cases.

In our experience ureteral strictures have always been associated with fibrous bands or adhesions. In several cases the strictures were actually surrounded by this tight fibrous tissue suggesting very strongly that the lesions were secondary, resulting from long continued pressure of the fibrous bands. Aberrant vessels have also been associated with ureteral strictures.

The pathological picture that results from a ureteral stricture depends on the site of the obstruction.   If the lesion is at or near the ureteropelvic junction hydronephrosis results.   On the other hand, if the narrowing

FIG. 7. Pyeloureterogram showing a large hydronephrosis and hydroureter. These were caused by several tight fibrous bands at the ureteropelvic junction, and by three small aberrant vessels crossing the upper, middle, and lower portions of the ureter respectively.

is in the lower ureter, one finds both a hydronephrosis and a hydroureter. The amount of hydronephrosis and hydroureter depends directly on the degree of obstruction and the length of time the obstruction has been

present. In long standing cases there is always considerable infection and stasis resulting in severe damage to the kidney.

The symptoms of ureteral obstruction are similar to those of obstruction due to bands or aberrant vessels. The principal manifestations are pain, pyrexia, urinary disturbances, with, at times, chills and fever, nausea

Fig. 8. Pyeloureterogram showing a moderate hydronephrosis on the right side. There is a definite filling defect at the ureteropelvic junction. At operation both a tight circular fibrous band and a definite stricture were found at the point corresponding to the filling defect.

and vomiting. Haematuria and a mass in the loin may also make their appearance.

The diagnosis of ureteral stricture depends upon all the data that can be obtained in the case. Thus a careful history, a thorough physical examination, several urinalyses, kidney function tests, and finally a cystoscopic examination, including ureteral catheterization and pyelography, are all essential in arriving at a correct diagnosis. Intravenous

pyelography is also a great aid and is used very frequently at our clinic. Cystoscopic examination is the most important single examination. If a stricture is quite marked the introduction of a ureteral catheter may be difficult. Further attempts with other types of catheter may be successful, and you then discover a definite hydronephrosis which can be

Fig. 9. Pyeloureterogram showing a moderate hydronephrosis and a very large dilated ureter. This was due to a definite stricture just near the ureteral orifice.

demonstrated by aspirating large quantities of urine from the renal pelvis. Pyelography will demonstrate a dilatation above the obstruction. If the narrowing is high a hydronephrosis only is present (Fig. 8); if the lesion is low both a hydronephrosis and a hydroureter can be observed (Fig. 9). Occasionally the stricture causes a complete transverse filling defect

in the pyeloureterogram, and in extreme cases the urographic substance does not pass beyond the obstruction.

The treatment of ureteral stricture is by operation, which may be either conservative or radical. The conservative method consists of repeated dilatations of the stricture by bougies. In a number of cases this form of treatment may be sufficient. The majority of ureteral strictures, however, require a more radical procedure. Exploration is carried out, and one of several plastic operations is decided upon. The Fenger operation consists of a longitudinal incision through the stricture with transverse suture according to the Heinicke Mikulicz principle for pyloroplasty. This operation has been praised by some and condemned by many. Herbst and Polkey have shown experimentally that, following this procedure, the opposite section of the ureter buckles. A more popular procedure is the utilization of the Rammstedt technique for pylorospasm. It was first applied to the ureter by Davis, and later by Vose, Bidgood and Roberts. This procedure consists of cutting longitudinally the strictured muscle down to the mucosa in one or more places. Others like Quinby and Walters recommend re-implanting the ureter into another portion of the pelvis. It must be remembered that ureteral strictures are usually associated with fibrous bands, and these have to be removed thoroughly before any form of pyeloplasty is carried out.

4. *Nephroptosis.* Renal ptosis, while not an uncommon finding, is, however, less frequently encountered than any of the above mentioned lesions. The condition is most commonly met with in thin children, and is usually associated with general visceroptosis. The right kidney is more often affected than the left one, although both organs may be ptosed. The condition is more commonly found in females.

In renal ptosis there is usually present a kink at the ureteropelvic junction (Fig. 10). This narrowing may be enhanced by a tight band or even an aberrant vessel. As the hydronephrosis develops, more nephroptosis results with increasing ureteral obstruction. Then the usual vicious circle is formed. If the obstruction is present for a long time infection supervenes and ultimately severe renal damage results. It is obvious that early recognition and treatment of the condition is essential.

The symptomatology of renal ptosis is not pathognomonic. Usually there are intermittent attacks of severe renal colic and the erroneous diagnosis of renal calculus is often made. At times the pain is dull in character, and may be present either in the loin or in the abdomen. If the discomfort is present in the right lower quadrant of the abdomen, appendicitis may be diagnosed. In late cases with infection there may be chills, fever, nausea, vomiting and pyrexia. Urinary symptoms, including haematuria, may also be prominent. Physical examination usually reveals a large, low, and tender kidney.

The treatment of renal ptosis must be undertaken before the kidney is irreparably damaged. Palliative measures may be resorted to. The

child is put to bed flat on the back for two to three weeks, followed by the wearing of a good abdominal support. If this treatment is unsuccessful then the proper procedure is nephropexy, including the removal of adhesions, and the straightening of the ureter. If a large hydronephrosis is present, part of the renal pelvis should be removed. After operation the child should be kept flat in bed for at least three weeks.

5. *Ureterocele.* By ureterocele one means the cystic dilatation of the lower end of the ureter due to a stricture or narrowing of the ureteral

Fig. 10. Pyelogram showing a moderate hydronephrosis on the right side in a low placed kidney. Note also the kinking and coiling of the upper third of the ureter.

orifice. This lesion must not be confused with the so-called prolapse of the ureter, which is really an eversion of the ureteral mucous membrane into the bladder.

Ureterocele is not common, but several cases have been reported in the literature. Recently Gibson discussed the subject and reported two personal cases. Campbell in 1934, mentioned eleven cases. Bilateral cases have also been encountered.

Ureterocele is believed to be the result of an anomalous development

of the lower ureter.   There are a number of theories regarding its origin.
The consensus of opinion is, however, that it results from the stenosis of
the ureteral orifice caused by the epithelial bar growing downwards to
separate the ureter from the primary excretory duct.

FIG. 11. Pyeloureterogram showing a large hydronephrosis and hydroureter.
A large ureterocele was observed on cystoscopic examination.

There are no symptoms that are characteristic of ureterocele.   Clinically
the picture is that of urinary obstruction, with or without infection.   In
long standing cases infection always supervenes, and the surgical lesion
is now one of pyonephrosis and pyo-ureter.   In bilateral lesions the
condition may become very serious, particularly when there is infection

present on both sides. The picture in these patients may be that of marked kidney damage with infection. Uraemia gradually develops and ultimately death ensues.

A positive diagnosis of ureterocele can only be made by a cystoscopic examination. By this procedure one definitely observes the lesion. A cystogram and pyelogram may also be taken, and usually are of considerable value (Fig. 11).

The treatment of ureterocele is to overcome the obstruction early and to establish adequate drainage. This form of treatment is carried out in cases where the kidney is not destroyed or badly infected. This conservative treatment consists of repeated ureteral dilatations by means of bougies. Where the ureteral orifice is very small it may be necessary to cut the orifice with either cystoscopic scissors, or a fulgurating electrode. In several cases none of these procedures are practical, and one may have to resort to fulguration and even excision of the cystic dilatation. In long standing cases where the kidney and ureter are badly damaged, a nephrectomy and complete ureterectomy is the proper procedure.

6. *Torsion of the Ureter.* Torsion of the ureter is rare and very few cases are reported in the literature. The torsion is usually at the ureteropelvic junction and in a number of instances recorded, there were also other congenital anomalies present in the genito-urinary tract. For example, Woelfler found a case of ureteral torsion associated with congenital valves in the course of the ureter. In our case there was a spiral torsion at the ureteropelvic junction on both sides, more marked on the right. In addition there was tortuosity of the right ureter in its upper third. Both ureters were dilated throughout and each had a stricture near the ureteral orifice (Fig. 12).

All writers believe that torsion of the ureter results from the persistence of the rotation of the Wolffian duct during its development (Eisendrath).

7. *Ureteral Calculus.* Calculus in the ureter is, of course, not a congenital anomaly. However, in the majority of cases it results from urinary stasis caused by a congenital obstructive lesion somewhere in the urinary tract.

Years ago calculus disease in children was commonly encountered. This was particularly true in Asia and several parts of Europe. With improvement of sanitation and dietetics the incidence of this disease has greatly diminished. Today in this country calculus disease in children is quite rare. Campbell in a series of five hundred and eighty children with a urological problem, found two ureteral and six renal calculi only. This finding has been universally true in all the clinics in this country.

The clinical history is that of a renal or ureteral colic which very often is associated with nausea, vomiting, or both. The urine nearly always shows gross or microscopic blood. The diagnosis is made on the history, physical examination, urinalysis, and finally X-ray examination. Cysto-

scopy with pyelography should always be performed (Fig. 13).   Intravenous urography may also be used and is usually a very valuable asset.

The treatment depends on the site and size of the calculus.   If it is high up in the ureter surgical removal is the procedure of choice.   If the calculus is small and low, ureteral dilatation will usually suffice.   On

Fig. 12. Photograph of casts of the renal pelves, ureters, and renal circulation. *Note* the spiral torsion of the ureteropelvic junction on both sides, more marked on the right.   *Note* also the tortuosity of the right ureter in the upper third.   Both ureters are dilated throughout, and each had a stricture near the ureteral orifice.

the other hand, if the stone is low but large, surgical removal is the proper treatment.

So much for the discussion of upper urinary tract obstructions.   Let us now turn to the lesions of the lower urinary tract that are responsible for urinary stasis.   In this group the obstruction may be found anywhere along the course of the urethra from the external urethral meatus to and

including the vesical neck. For the sake of clarity the lower urinary obstructions may be divided into two groups, namely those found in the anterior urethra and those in the posterior portion.

The most common obstructive lesions of the anterior urethra are:

1. Meatal strictures.
2. Stenosis of prepuce.
3. Stricture of anterior urethra.

Fig. 13. Photograph of X-ray plate showing elongated calculus in the lower third of ureter in a female, aged seven years.

We are purposely omitting the acquired lesions, such as acute gonorrhoeal urethritis, urethral stone, traumatic rupture of the urethra, etc.

1. *Meatal Stricture.* This congenital anomaly is very common and occurs both in males and females. In a urological clinic, however, many more males are seen.

The symptoms complained of are difficulty in urination, small stream, and frequency. Very often the stricture is so marked that the child has

to strain every time he voids. Occasionally a child is brought to the clinic because he has a bloody discharge from the urethra. This discharge may close the meatus and cause complete retention. The treatment is a meatotomy which usually corrects the condition.

2. *Stenosis of Prepuce.* This malformation is another common congenital anomaly. If the stenosis is extreme there is considerable difficulty in urination with pain and frequency. The prepuce is very often inflamed and there is present an associated purulent balanitis. Long standing cases with marked stenosis of the prepuce may cause urinary stasis and back pressure in the bladder and kidneys, with serious results. Campbell reports four such cases that died of uraemia. These children should all be circumcised at birth.

3. *Stricture of the Anterior Urethra.* This type of obstruction is usually associated with meatal stricture. The obstruction is really a narrowing of the entire lumen of the anterior urethra. The symptoms are difficulty in urination, small urinary stream, and frequency. The condition should be recognized early and repeated dilatations with sounds usually suffice.

OBSTRUCTIVE LESIONS OF THE POSTERIOR URETHRA AND VESICAL NECK

These conditions are not uncommon and give rise to clinical pictures which simulate those observed in older men suffering with prostatic obstruction.

The children usually complain of frequency, urgency, difficulty in urination, small stream and hesitancy. At times there is dysuria and even haematuria. Several of these children have incontinence, and a diagnosis of functional enuresis is frequently made. In advanced cases there is residual urine, infection, and signs of renal insufficiency. If the obstruction is not removed uraemia eventually sets in with death ensuing shortly after.

The bladder may show trabeculations and even diverticula. The ureters are dilated and there is bilateral hydronephrosis present. In late cases the kidneys are destroyed, and now the picture is that of a bilateral pyonephrosis and pyo-ureter.

The urine nearly always contains a great deal of pus, many bacteria, and microscopic blood. If there is a residual urine present, the reaction of urine may be alkaline.

The most common obstructions of the posterior urethra and vesical neck are:

1. Contracted vesical neck.
2. Posterior urethral valves.
3. Cysts.
4. Hypertrophy of the verumontanum.

1. *Contracted Vesical Neck.* This type of obstruction has been recognized for a long time. It is due either to a muscular hypertrophy or a

fibrosis of the vesical neck. Occasionally this lesion is associated with obstructing folds of mucous membrane. Urinary difficulty from birth should make one consider the possibility of a contracted vesical neck, and the proper urological investigation should be carried out. The importance of early recognition is obvious. In the routine examination of the genito-

Fig. 14. Cystogram in a male child, aged seven years, with a contracted vesical neck. *Note* the large bladder with many small diverticula.

urinary system it may be found that a soft rubber catheter, even a French No. 8, will meet obstruction at the vesical neck. It may be necessary to use a filiform to overcome this contraction. Large quantities of infected residual urine, which is usually alkaline, may be withdrawn.

A cystogram will reveal trabeculations and diverticula (Fig. 14), and very often there is evidence of reflux up one or both ureters, which are

usually markedly dilated (Fig. 15).   The obstruction of the vesical neck
may be removed either by repeated dilatations with sounds, or by resec-
tion.   At times both methods are used.

Fig. 15. Pyeloureterogram bilateral in the case just described (Fig. 14). *Note*
the large hydroureters.

2. *Valves of the Posterior Urethra.*   Posterior urethral valves are quite
common, and the lesion should be considered in all cases of urinary diffi-
culties in male children.   Young in 1912, observed the first case cysto-
scopically and removed the obstruction by operation.   Several cases have
been reported since.   In 1934, Lowsley and Kirwin reported on one
hundred and thirty-three cases.   In 1937, Fagerstrom collected ten addi-

tional cases and added four of his own, making a total of one hundred and forty-seven. We have observed one case at the Children's Memorial Hospital.

The valves vary in size and shape. They may consist of simple mucosal folds or ridges, or they may take the shape and form of definite fibrous diaphragms. Young and his co-workers report three distinct types.

Type 1. The valve consists of a ridge on the floor of the urethra, running from the verumontanum anterior to the bulbomembranous urethra. Here it either divides into two processes which merge with the lateral urethral walls, or it completely encircles the urethra.

Type 2. Here the valves run from the verumontanum posteriorly to the bladder neck.

Type 3. This is the iris valve, and may be found anywhere in the posterior urethra.

The diagnosis of urethral valves can be made by cysto-urethroscopy. At the same time the bladder will show trabeculations, diverticula, and marked inflammation. Pyelography, whether retrograde or intravenous, will usually reveal large dilated ureters and renal pelves.

When treatment of these children is considered, the same principles that are applied to older men suffering with chronic urinary retention must be observed. The bladder must be emptied gradually and drainage continued until the renal function improves. This may usually be done by an indwelling soft rubber catheter, although occasionally a suprapubic drainage may be necessary. The patient must be given large quantities of fluids, and other forms of eliminatory treatment are to be carried out. When the general condition of these children improves, as evidenced by better kidney function, cleaner urine, improved appetite, and gain of weight, the question of surgical interference may be considered. The object of the treatment is the removal of the obstructing valve.

In the majority of cases fulguration of the obstruction through the operating cystoscope is the ideal method of approach. In rare instances where urethral instruments cannot be passed, the valves may be removed through a suprapubic cystotomy. Some surgeons advocate urethral dilatation only. In our case fulguration through the operating cystoscope was successfully carried out.

Postoperative treatment of these cases is quite important. Some surgeons leave a urethral catheter in situ for several days; others dilate the urethra periodically to prevent scarring at the point of fulguration.

It must be appreciated that in late cases treatment of this lesion or of any other type of urethral obstruction will not restore the urinary tract to its normal state. Irreparable damage has been done and restoration to integrity will never take place. It is true that the clinical symptoms will be alleviated, the kidney function will improve, infection will be less marked, and the general condition of the patient will be much better.

On the other hand, however, the diverticula of the bladder, the large dilated ureters and pelves, will remain unchanged indefinitely. This is due to the fibrous replacement of the musculature resulting from the long standing back pressure and infection. So briefly, what we hope to accomplish with our treatment is an improvement in the general condition of the patient, both symptomatically and clinically, and the prevention of further damage to the urinary tract.
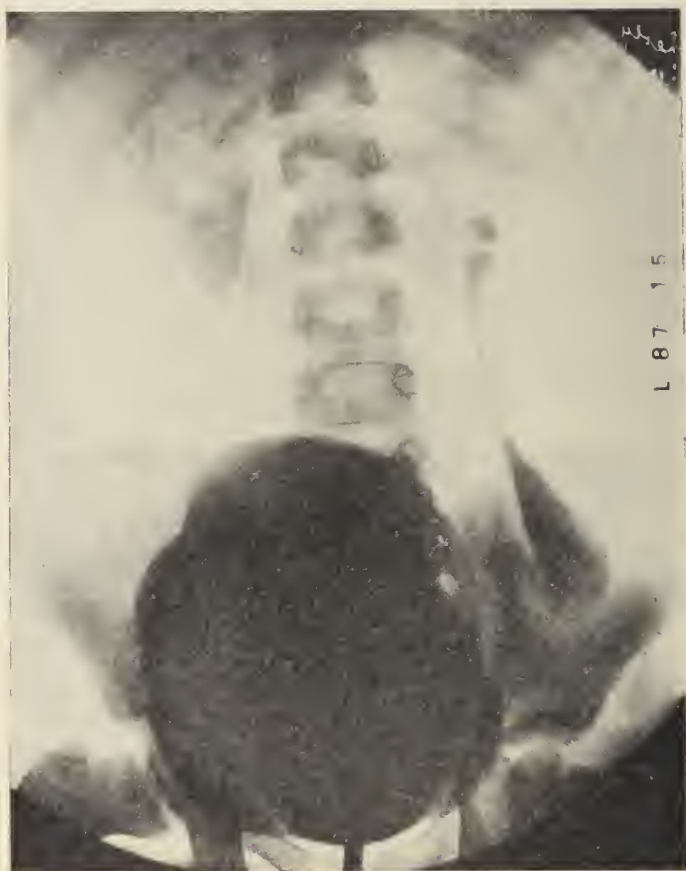
FIG. 16. Cystogram in a male child, aged nine years, with a cyst of the posterior urethra. *Note* the large irregularly shaped bladder with reflux of the dye up both sides. *Note* also the large right hydronephrosis and the markedly dilated left ureter.

3. *Cyst of the Posterior Urethra.* This condition must be very rare. Campbell does not mention the condition in his papers. Eisendrath just refers to the congenital valves and hypertrophy of the verumontanum in children. Our reason for mentioning the lesion is that we encountered such a case. The diagnosis was made at autopsy. The clinical history and findings were those of a posterior urethral obstruction with severe

Fig. 17. Photograph of the posterior urethra and part of bladder in the case just described (Figs. 2 and 16). *Note* large cyst bulging into the posterior urethra.

renal destruction, insufficiency and infection. Dr. Chase of the Department of Pathology, Royal Victoria Hospital, has made a thorough study of the case, and believes that the cyst resulted from a congenital stenosis of Cowper's duct. This caused distention which gradually extended

backwards through the posterior layer of the triangular ligament and bulged upwards in the prostatic urethra (Figs. 16 and 17).

4. *Hypertrophy of the Verumontanum.*   This lesion is less common than urethral valves.   The condition is very often undiagnosed, and several cases have been observed at autopsy.   Cases have been discovered in stillborn children, and were associated with bilateral hydronephrosis and hydroureter, and destroyed bladders.   If the lesion is not recognized early the children become undernourished, pale, dull, and eventually uraemic.   Death ensues very shortly after.   The most satisfactory form of treatment is shrinkage by the dessicating current.

SUMMARY AND CONCLUSIONS

1. Obstructive lesions of the urinary tract in children are usually congenital, resulting from anomalous development.

2. Obstructions in children are found both in the upper and lower urinary tracts.

3. All children with pyuria should have a thorough urological examination.

4. The importance of early recognition and treatment of urinary obstruction is stressed.

5. Treatment of urinary obstruction must be executed before advanced destructive damage to the genito-urinary tract has taken place.

6. The most common obstructive lesions of the urinary tract in children are briefly discussed.

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THE CONSERVATIVE TREATMENT OF LARGE HYDRONEPHROSES

Plastic Procedure and Fixation of the Kidney*

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What is meant by the term 'large hydronephrosis'? A hydronephrosis can be considered large when it admits one hundred cubic centimeters of fluid or more. In some cases the capacity is very much larger than this and may reach three hundred cubic centimeters, five hundred cubic centimeters, or a litre. In these hydronephroses the renal parenchyma is fatally damaged. Dilatation of the renal tubules is followed by peritubular and periglomerular sclerosis, so that the parenchymatous structures may disappear completely. It is important, however, to realize that when obstruction is removed these hydronephrotic kidneys may resume a considerable degree of function and may suffice to keep the patient alive.

Large hydronephroses develop altogether latently until such time as complete obstruction, infection or hematuria leads to their discovery. Indeed, if these hydronephroses caused pain—as happens in the ordinary variety—the patients would seek relief earlier and necessary measures would be instituted.

Why do large hydronephroses fail to produce pain? The reason probably is that the obstacle to urinary drainage, though permanent, is incomplete, so that a painful state of tension is not created.

When at any given time the lesion, in consequence of some complication, is brought to eventual recognition, the volume of the hydronephrosis can be determined by means of pyelography. Whenever a hydronephrosis is encountered it is essential for the physician to make pyelograms of *both* kidneys, since in two-thirds of the cases hydronephrosis is bilateral. This bilaterality may determine what treatment should be applied to the hydronephrosis which attracted attention in the first instance.

In general, slightly large hydronephroses are too frequently removed. This is done because the bilaterality is often overlooked and because the physician insufficiently realizes that a hydronephrotic kidney, despite great dilatation, may regain a considerable part of its function. In my opinion the treatment of large hydronephroses should not necessarily

consist of nephrectomy. So long as the function of the renal parenchyma is still appreciable the kidney should be conserved, according to the method which I shall presently describe. This conservatism is indispensable when voluminous hydronephrosis is present on both sides. Quite often I have saved a hydronephrotic kidney which had been marked for removal; although naturally enough the shape of the pelvis and calyces did not return to complete normality, the symptoms almost always ceased, and the patient retained a kidney which possessed diminished but appreciable function. Only in exceptional cases have I been obliged to remove such kidneys subsequently.

Hence I insist on the necessity of not removing a large hydronephrosis as a matter of routine. On the contrary preservation should be attempted especially if the opposite kidney is also hydronephrotic.

What should be done to preserve a large hydronephrosis?

The first occasion I had to treat a case of this sort was in 1910. The patient, a woman, had been sent me by Dr. Benoit. At that time few pyelograms were being made. I found a somewhat large and mobile left kidney which gave rise to painful crises. I proposed to perform fixation of this kidney.

During the operation I found the kidney and pelvis to be greatly dilated. I had a momentary inclination to remove the kidney. However, since I had not originally intended to do a nephrectomy, I had not explored the opposite side. Not knowing what to do, I elevated and fixated the kidney and drained it by nephrostomy.

Some weeks later I removed the drain of nephrostomy. In a few days the fistula closed. This closure proved that the outlet was completely free and that the ureteral kink caused by ptosis of the kidney had disappeared. The patient was definitely relieved of his symptoms.

This chance observation led me to try the method regularly in cases of large hydronephrosis. I have had opportunity to perform the operation in a number of cases, almost always with the same result.

Thus it seems that in these cases preservation of the kidney should be attempted in the manner which I suggest: removal of the obstruction, followed by high fixation and drainage of the kidney. Drainage is discontinued after it has allowed the kidney to contract and to rid itself of any infection which may be present.

Pyelograms made via the drain in the kidney enable the surgeon to study the postoperative evolution of the hydronephrosis. As long as the pelvis continues to shrink, the drainage should be maintained. When two pyelograms taken several weeks apart show no further reduction in the pelvis, the drain may be removed. At this time one of two things will happen. As a rule the fistula will close, proving that the urinary passages are patent. However, if the fistula persists it will be necessary to decide whether the further preservation of the kidney is necessary for the life

of the patient (i.e. if the opposite kidney is insufficient); otherwise, if the opposite kidney is competent, the fistulous kidney may be removed.

It must not be supposed that after these operations the kidney and pelvis return to their normal size and shape. They remain permanently dilated, although smaller than they were during the period of obstruction. However, the dilatation has no tendency to increase, the urine flows

Fig. 1. Hydronephrotic kidney—preoperative pyelogram

normally, symptoms are absent, and the kidney functions as well as its remnant of parenchyma will permit.

There are cases in which the kidney is so large that removal of the obstruction and fixation of the organ are impossible. Under these circumstances nephrectomy must be performed if the opposite kidney is competent. If it is incompetent or absent permanent nephrostomy must be performed. In these cases one is often astonished at discovering that a

kidney which might have been considered worthless because of the slenderness of its surviving parenchyma may prove sufficient to maintain life.

Even when acute infections supervene in a very large hydronephrosis nephrectomy must be regarded with great caution.   It is not so much because the infected kidney produces serious symptoms that it must necessarily be removed.   If there is enough time for suitable study of the case and if the opposite kidney is good, the suppurative pocket may be removed at once, provided this can be done without too much difficulty. Otherwise it is merely opened until the acute phase has passed, after which it is removed.   If the opposite kidney is incompetent, nephrostomy is kept permanently.

Here is an example of what can be done by drainage of the kidney combined with fixation.

The patient was a young man of 26.   Since his adolescence he had been treated for colitis.   On one occasion he had hematuria.   A pyelogram showed the presence of a large renal pouch on the left side (fig. 1).   On the right side a hydronephrosis was also present but it was much smaller than that on the left.   I therefore decided to preserve the left kidney, which was the site of the very large hydronephrosis.   At this time examination of the urine showed the following:

	Right Kidney	Left Kidney Pus and B. Coli
Urea	18.15	7.9
P.S.P	32%	20%

At operation I found marked dilatation of the kidney and pelvis. Below the pelvis there was an inferior polar artery, which I cut.   I then lifted up the kidney and placed a drainage tube in its greatly dilated lower pole.   I left this drain in place for three months.   Each month I made a pyelogram, using a catheter in place of the drainage tube.   After the fourth pyelogram (fig. 2) the pelvis stopped shrinking and I removed the drain.

Several days later the lumbar fistula closed.   After this time the patient had not the least trace of kidney pain.   At this time examination of the urine showed:

	Right Kidney	Left Kidney Pus and B. Coli
Urea	14.25	10.6
P.S.P	30%	24%

Thus a marked improvement had taken place in the function of the left kidney.   Evidently it will not return to a normal level of function, but during the eighteen months which have elapsed since the operation the patient has had no pain in his side, and he will keep a very useful kidney.

Concerning the treatment of large hydronephroses, I shall describe the technique which I use for fixation of the kidney.

This method of reposition of the kidney is commonly called nephropexy. The term is inaccurate because it does not indicate the essential fact that the kidney must be fixed *high* in order for a good result to be obtained. The operation is one which formerly had the worst reputation possible; since it has been more properly performed it has become more and more popular. In 1913 I had one of my internes, Luzoir, write a thesis on this operation which was then very much in disrepute. After seeking out

FIG. 2. The same case as in figure 1. Pyelogram (retrograde), four months after operation

the patients on whom I had operated, Luzoir concluded that all, or nearly all, the patients had had either complete cure or at least considerable relief. Since that time I have insisted that in order for a good result to be obtained *it is necessary to fixate the kidneys very high and very firmly.* Since then this opinion has been generally accepted and the results obtained by high fixation of the kidneys are now among the best in surgery of the urinary tract.

I shall not describe here the operation which I use in cases of moderate hydronephrosis. I shall describe only the methods used in cases of very large hydronephrosis.

1. Mobilization of the Kidney. The first stage of reposition of the kidney consists of exteriorization. The kidney is approached by the classical incision which passes from the lumbo-costal angle to a point situated about three fingerbreadths above and medially to the anterior superior iliac spine. The abdominal wall being incised, the lumbar area is exposed.

This lumbar area is bounded by an aponeurosis and forms the posterior wall of the kidney bed. In the supero-posterior quadrant of this wall the aponeurosis is incised with a bistouri. When the kidney bed is penetrated in this way the kidney is reached.

The kidney being found, it is pulled over and freed from surrounding connective tissue and fat, to which it may be adherent. When the hydronephrosis is great the pelvis can be seen to make a more or less distinct anterior bulge. The entire kidney must be carefully isolated and liberated from the surrounding tissue and the intestine must be carefully separated, especially on the right. Finally this process will permit the complete liberation of the more or less enlarged kidney and pelvis.

2. Examination of the Pelvis and Ureteral Region. This examination is essential, for frequently an abnormal vessel can be discovered, which passes in front of the ureter and may kink it. This abnormal inferior polar vessel goes to the lower pole of the kidney. After it is found it is cut between two ligatures.

If this vessel is not found the pelvis and upper part of the ureter must be carefully freed from the surrounding connective tissues, which sometimes adhere and produce bends in the ureter. The ureter must be made entirely free to assume an absolutely straight course. The ureter must also be freed from many adhesions which it has made with the lower part of the greatly dilated pelvis.

3. Plication of the Pelvis. When the hydronephrosis is very large, the ureter instead of entering the lower part of the pelvis may enter at a much higher level, even at the very top. Below this there will be a pelvic recess which is often important and difficult to evacuate. In these cases the recess must be closed by pleating the wall of the pelvis by means of very fine threads which do not go through to the interior (fig. 3). This plication may be made either by means of interrupted sutures or by a purse-string suture which is passed completely around the bulging part of the pelvis. The part of the wall situated in the middle is pushed back into the pelvis. It is advisable to perform this plication with non-absorbable sutures, such as linen threads.

4. Removal of Strips and Placement of the Fixation Sutures. In these very large hydronephroses it is advisable to tilt the kidney so that the

hilum will face downward and the ureteral orifice will be situated at the lowest point. The method of *Surraco* of Montevideo is successful in this regard and is in addition very easy to carry out.
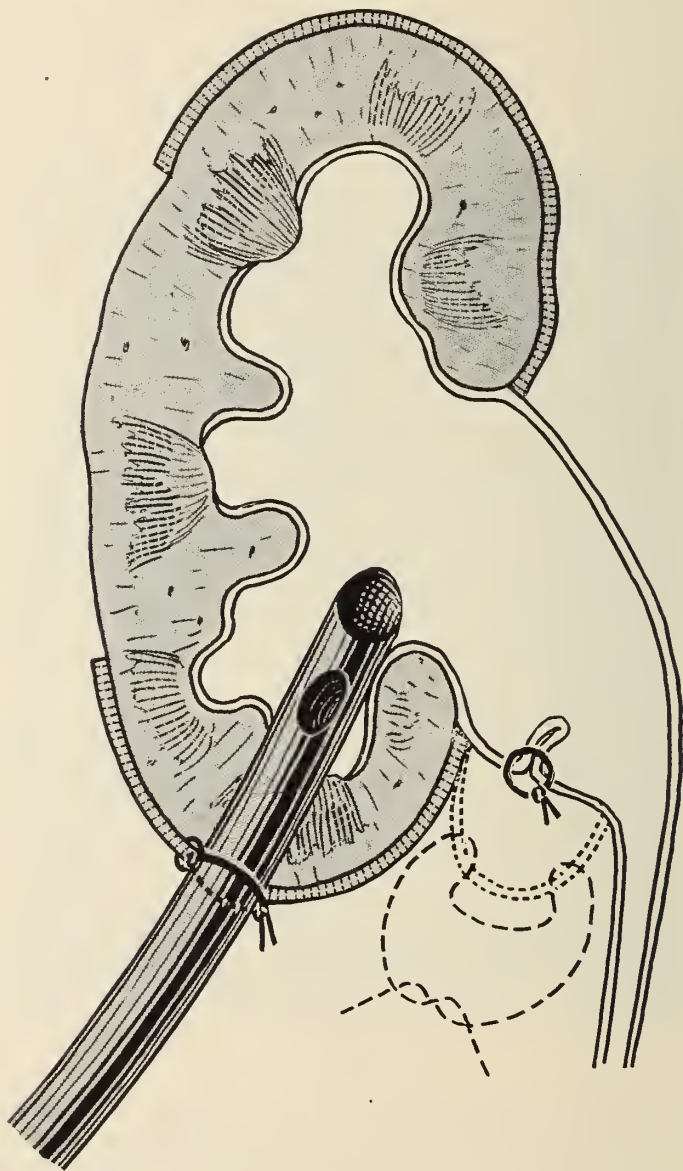
FIG. 3. Schematic drawing showing plication of the pelvis with drainage tube in lower calyx

In order to perform fixation by this method two strips are made at the external border of the kidney by means of a median incision which
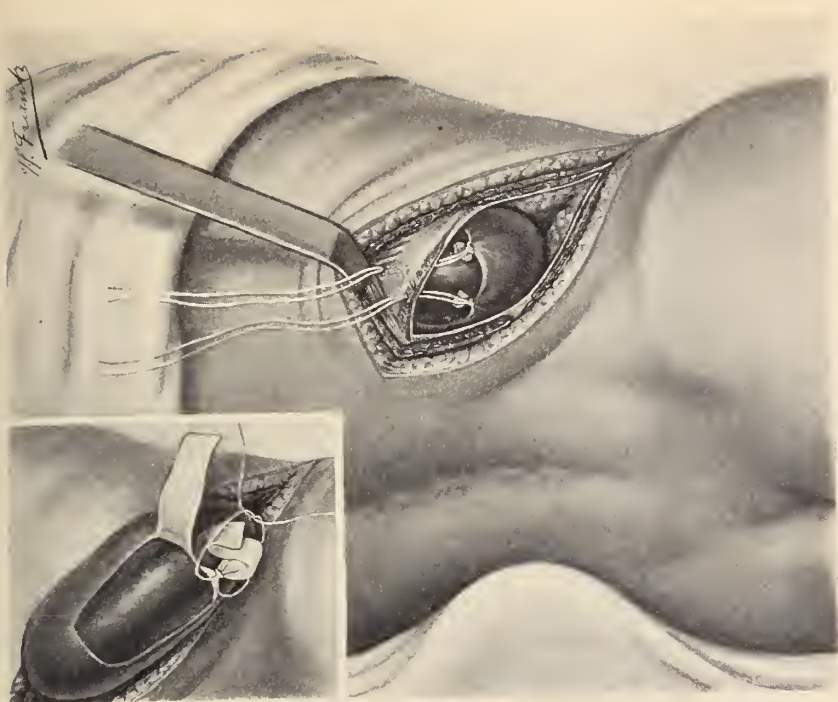
Fig. 4. Mode of fixation of the kidney following the procedure of *Surraco* by means of two strips.
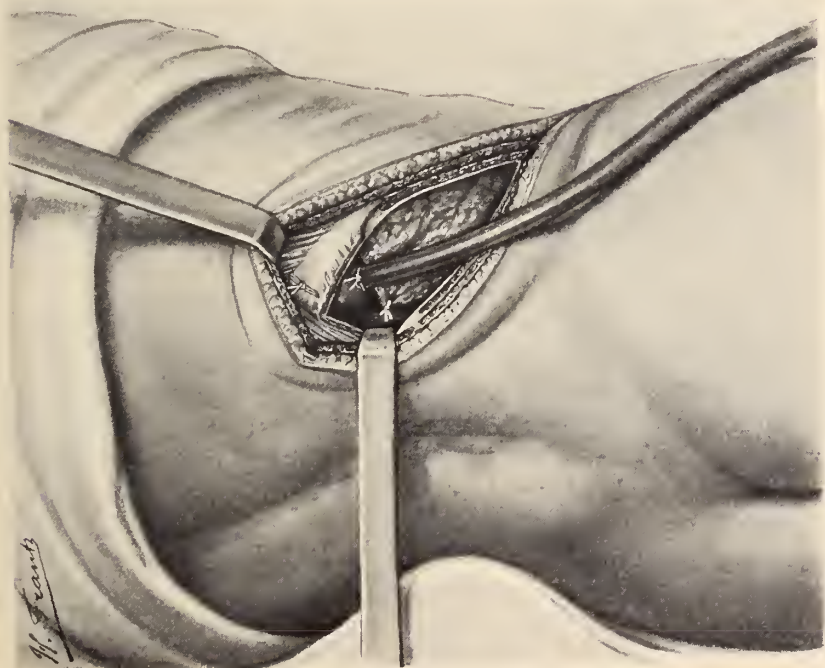
Fig. 5. Drawing illustrating the fixation and drainage of the kidney and its re-enforcement by the formation of a "hammock" of perinephric fat

passes along the external border of the kidney and two lateral incisions parallel to the median incision (fig. 4). These vertical incisions are connected above by a horizontal incision. The lower end of the incisions should be about a finger's distance above the lower pole. The vertical incisions should be about three centimeters apart so as to make the large and firm capsular strips. By means of these incisions it is possible to remove two longitudinal strips which are used for fixation.

The base of each of the strips is closed by a linen thread which is then tied around this foundation, the strips themselves being caught in the knots. These are the threads which will serve for fixation.

5. *Placement of the Sutures on the Thoracic Wall.* The sutures placed on the strips are passed some above the twelfth rib, the others below it, and two main threads of the same strip are tied to the main threads of the other strips, while the assistant lifts the kidney as high as possible.

6. *The Drainage of the Kidney.* Once the kidney is fixed in this way, the renal capsule is very lightly incised with a bistouri at the tip of the lower pole. A clamp placed in this incision will easily pass through the renal parenchyma into the pelvis, which is greatly dilated. The removal of a few pieces will enlarge this incision a little. Through the orifice thus made a kidney drainage is placed; this is fixed by catgut strips to the renal capsule. To complete the fixation, the perinephric fat is placed below the kidney; through this tissue a suture is placed and is tied to the muscles of the lumbar wall (fig. 5).

7. *Closure of the Wound.* The wound is closed in the usual way and an extrarenal drain is kept in place for several days. The other drain which passes to the kidney is fixed to the skin.

Subsequent Treatment. After a few days the extrarenal drain may be removed. The wound will cicatrize completely. The kidney drain is left in place as long as possible; its end must go well beyond the dressing. Two or three weeks after the operation, if the drain is blocked it may be replaced. The drain may be replaced by means of a Pezzer catheter which will keep itself in place better than an ordinary drain.

As I have said above, pyelograms can be made through this drain for the purpose of studying changes in the size of the pelvis. It is only when these pyelograms show that the pelvis has stopped shrinking that the drain is withdrawn. The urine thereupon immediately passes through the ureter. If the fistula closes promptly the ureteral passages are packed.

PERFORATION OF THE URETER*

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Diagnostic errors and therapeutic failures are seldom published. The case which I am about to report, in a way, represents a failure, even though the final result was good. The pathogenesis in this case is not fully understood, yet, for various reasons, I consider this case worth reporting.

CASE REPORT

History. A girl of 22, college student, consulted me for the first time in February, 1930, complaining of colicky pains in the right side of the abdomen. One month before I first saw her, the patient had suffered from a typical renal colic with dark urine and a rise in temperature. Cystoscopy showed clear urine and a normal bladder; there was no difference in the appearance of the two ureteral orifices. X-ray examination revealed a cylindrical shadow suggesting a calculus, situated in the pelvic part of the ureter. The urine was clear, but contained bacteria, and, during the attacks, was at times slightly bloody. Repeated probings of the right ureter demonstrated an obstruction about 2 centimeters beyond its orifice. On one occasion the catheter could be passed beyond this point. Several futile attempts were made to mobilize the calculus by ureter catheterization and subsequent injections of glycerine and lapis. The condition remained unchanged until October. Once or twice a month, the ureter was catheterized. Once in a while, colicky pain appeared, which now however, was regularly associated with high temperatures. Such rises in temperature sometimes also followed ureteral catheterization, which otherwise caused few subjective complaints. In November, with the temperature remaining elevated for a long period, operation became urgent. For several months I had complied with the request of the patient and deferred operation in the hope that the calculus would be passed spontaneously. Radiographic examinations at this time —both flat plate and intravenous pyelogram—showed no change in the position of the calculus and no marked dilatation of the upper urinary passages on the right side. But on December 5 an intravenous pyelogram showed the pelvic part of the ureter to be definitely dilated; both kidney pelves were normal and excretion of the dye was unimpaired (fig. 1).

As the temperatures subsided somewhat, the patient was given cylotropin intravenously daily for several days. Finally the patient was subjected to operation on December 12, 1930.

Operation. It was done under ether anesthesia. The incision was typical, from the superior anterior iliac spine to the midline. Where the incision crossed the vessels, the ureter which was dilated and embedded in thick adhesions, was exposed and was dissected downward. No calculus

Fig. 1. Radiogram December 5, 1930

could be found by palpation. Toward its lower orifice, the ureter narrowed. Here the ureter was incised. Again, no calculus could be palpated from the outside. Even when a probe and later a forceps were introduced into the ureter and pushed both in a cranial and caudal direction, no calculus was encountered. A ureteral catheter could be passed upwards toward the kidney without difficulty. A second such catheter was passed downward, and entered the bladder, which fact was at once established cystoscopically. In addition, a ureteral catheter inserted

into the cystoscope, now passed without obstruction, and appeared in the incision. The operation consumed an unusually long time, and finally had to be terminated because of the poor condition of the patient. The ureter was closed by paramucous stay sutures; drainage tubes were left in situ.

Postoperative course. The first days after operation were stormy. The patient was in profound shock and cardiac function was poor. The dressings were profusely saturated with urine. The urine output by the natural passages, however, was sufficient. Gradually, the patient's condition became more stable, and the temperature as well as the pulse became normal. Only the condition of the operative site still left much to be desired. There was a fistula of the ureter and all the urine produced by the right kidney was discharged through this fistula. Several weeks following the operation, the rubber drain which led to the ureter and carried the urine, discharged solid particles which looked and felt like phosphates. Within a few days, they formed a considerable quantity and filled a test tube.

On January 28, X-ray examination showed small concrements in both the right and left kidneys and in the right ureter (fig. 2). Immediately after the operation, we had used cylotropin intravenously on and off, but now, the urine was acidified by oral medication. Radiograms, as shown in figure 3 of February 16, and in figure 4 of February 19, disclose that the catheter does not reach the cylindrical calculus. When studying earlier radiographs, the possibility that the calculus might be situated outside of the ureter was considered. The intravenous pyelogram showed considerable dilatation of the right renal pelvis and right ureter (fig. 4). The radiogram in figure 5 of March 26, shows fewer concrements in the right kidney, but more, further down in the right ureter. The left kidney no longer shows calculi. The radiogram in figure 6, of April 29, 1931, compared with the preceding radiogram, shows an increase in the number of calculi in the region of the right ureter; in the right kidney only one small calculus remains demonstrable; no more calculi are visualized on the left side.

The patient had made a complete recovery, was consistently afebrile, and had no pains whatsoever; the entire urine output of the right kidney was discharged by way of the fistula.

It seemed to me that spontaneous closure of the fistula could not be counted upon. Besides, for obvious reasons, I objected to another attempt at removing the ureteral calculus by operation. Leaving all other considerations aside, such an attempt appeared too risky to me because of the badly infected condition of the tissues in the operative site. I, therefore, proposed nephrectomy, which was done on May 30, 1931.

Second Operation. The operation was simple. A flaccid kidney was found. Examination of the organ revealed chronic pyelonephritis with

FIG. 2. Radiogram January 28, 1931   FIG. 3. Radiogram February 16, 1931

FIG. 4. Radiogram February 19, 1931   FIG. 5. Radiogram March 26, 1931

beginning contraction. For the reasons just mentioned, I avoided traversing the badly infected tissues of the previous operative site, and dispensed with ureterectomy.

Convalescence. The operation was followed by uneventful recovery. The fistula of the ureter closed spontaneously; the scar at that site showed marked retraction. The patient felt perfectly well and had no complaints. The urine was clear but mild bacteriuria persisted.

After a considerable interval, the patient, who, in the meantime, had taken her doctor's degree, presented herself again. She looked a picture of health, felt well and actively engaged in sports.

Fig. 6. Radiogram April 29, 1931

On February 7, 1933, another X-ray study was taken (fig. 7). It shows the cylindrical shadow previously seen, and, in addition, numerous round shadows, of lentil size and smaller, arranged like a string of pearls. These shadows reach up to the level of the second lumbar vertebra. Just above the symphysis, several smaller irregular shadows are visualized, which might correspond to inspissated, calcified pus.

A check-up X-ray study on November 7, 1934, showed about the same picture as seen in figure 7.

Shortly thereafter, the deeply retracted scar at the site of the original

FIG. 7. Radiogram February 7, 1933

FIG. 8. Radiogram January 12, 1935   FIG. 9. Radiogram January 19, 1935

ureteral fistula opened spontaneously. A thin discharge, mixed with solid particles, appeared. A fistula with an opening of pin-head size remained patent for some time. While this condition lasted, on January

12, 1935, I took an X-ray picture with the ureter catheter inserted into the fistula. Figure 8 shows a marked diminution in the number of the small, bead-like calculi, and a noticeable change in the position of the primary cylindrical shadow. Several other shadows on the left side of the pelvis had also changed their position.

On January 19, 1935, I again injected contrast material through a ureter catheter which was inserted into the fistula. In figure 9, it is

Fig. 10. Radiogram February 23, 1935

demonstrated clearly that the calculi are situated in the retrovesical tissues. This was more apparent when examination in the lateral position was made. On February 23, 1935, I did a retrograde filling of the stump of the ureter. The catheter could be inserted for a distance of two centimeters. In figure 10, the ureter appears filled up to the level of the third lumbar vertebra. Within the shadow of the ureter, filling defects are demonstrated which correspond to calculi situated in the ureter.

SUMMARY

The case is one of calculus of the ureter which, in spite of its size, could not be located at a typical operation. A fistula of the ureter remained through which all of the urine of the respective kidney was discharged. During the first few weeks, a considerable number of phosphate calculi formed above the original calculus, in the ureter, in the kidney of the same side, and in the healthy kidney. During the further course, phosphate particles continued to be discharged through the fistula. The shadows in the right kidney decreased in number; the shadows in the healthy kidney disappeared. Following nephrectomy, the fistula healed. The remaining calculi in the ureter caused no more symptoms. Much later, the scar opened, thin pus with solid particles was discharged and X-ray examination revealed that a number of the ureteral calculi must thus have passed. But besides, it was also demonstrated that the large calculus as well as a number of the smaller ones were situated in the retrovesical tissues, outside of the lumen of the ureter. This should have been suspected much earlier.

COMMENT

This case seems unique enough to me. In the first place, we need an explanation why the calculus was not found at the first operation. Was it already outside of the ureter at that time? One fact may speak against this possibility. An intravenous pyelogram taken shortly prior to the first operation showed dilatation of the ureter above the calculus. Nevertheless, it is possible that the calculus perforated at some time between pyelography and operation. The calculus may well have tamponaded the site of perforation. That the ureter ruptured at a site where its wall was normal, is hardly possible. There probably were dense adhesions, which, incidentally, prevented infiltration of the surrounding tissue with urine.

According to reports published in the literature, rupture of the ureter usually does not produce dramatic manifestations. An occurrence such as closure of the site of perforation by the calculus has been described.

Still another possibility would be the following: the manipulations during the operation, while the calculus was looked for, might have led to perforation. Such an explanation has much to commend itself. It would, for instance, explain why, at operation, a ureteral catheter inserted from the bladder passed the ureter and appeared in the wound without meeting an obstruction. Lastly, there is a possibility that at some time following nephrectomy, perforation occurred. Such perforation would have been well prepared by pressure necrosis of the ureteral wall produced by a calculus which remained in place for a long time.

In any event, the delay of the first operation for removal of the ureteral calculus must be considered a mistake, even though I am convinced that

the delay of the operation in itself cannot be blamed for our failure to find the calculus.

I admit that the case was not clear to me at all. I am well familiar with difficulties encountered during an operation for ureteral calculus. It probably has happened before that a surgeon has failed to find a calculus, but such unpleasant occurrences are usually not reported in the literature. Besides, I must admit that I was unaware of the perforation of the ureter by the calculus. Neither did I know that extraureteral position of calculi, while infrequent, is not extraordinarily rare—I learned this only from reviewing the literature. Yet, I, myself, once wrote a paper on rupture of the bladder, and in another paper, I reported a war-time case, where I found a renal calculus in an ordinary abscess of the back. Gottstein, in his excellent monograph on nephrolithiasis, published in Handbuch der Urologie, discusses perforation of the kidney and the kidney pelvis into the surrounding tissue and into other organs. He also mentions perforations of the ureter which are no rarer than perforations caused by renal calculus. The most comprehensive papers on the subject are those by Frenkel, Köhler and Lion.

To the pathologist, the passage or perforation of a calculus from the ureter into the surroundings, is easily understandable. Whether this event leads to dramatic manifestations or not, depends only upon local conditions. Judging by reports in the literature, it usually did not result in very acute symptoms. This was the case in our patient also. The calculus originally situated within the ureter later was found outside of the ureter. Now, it is not essential to know whether this was the case as early as 1931, when we first suspected it, or in 1935, when we found the concrements lying definitely not in the ureter but in the retrovesical tissues, and then they appeared to be movable. The site of the perforation as well as its direction, of course, depend upon local conditions in each case. Perforating calculi have been found partly within the ureter and partly outside of it in the psoas muscle (Blake). In other cases, the calculus had left the ureter completely, and was situated outside of the ureter and adjacent to it (Barry, Marion). In a case published by Johnson, the calculus lay in a retroperitoneal abscess. Godler found it under the skin of the lumbar region. Barry and Bächer encountered it in the inguinal region. Lion found it above the iliac crest, and Albarran in the thigh and buttocks. Abscesses subsequent to perforation of the ureter which ruptured into the rectum have been reported (Kern, Berard and Bussy, Thompson and Spencer Wells). In the cases published by Brentano and by Bach-Egan, the calculus was found in an abscess which had to be opened through the bladder.

Embedding of calculi in the periureteral tissues has also been described (Marion, Reuter).

It appears—and it is confirmed by Köhler's review—that the perfora-

tion usually occurs at a site where the calculus in the course of its long stay had produced fibrosis. A decubital ulcer must precede perforation. In rare instances, a diverticulum-like niche of the ureter with thinning of the wall (pressure-atrophy) has been observed. (Tedenat, Jeanbreau.)

When we contrast the frequency of renal calculi and especially of ureteral calculi with the rarity of rupture or perforation of the ureter—whichever term you prefer to use for the phenomenon—we must perhaps bear in mind that some predisposing cause might be present; the fact that the calculus lodges in the ureter, in itself does not account for it, or else rupture would be more frequent. It is tempting to assume the existence of predisposing factors, yet even such an hypothesis would not suffice to excuse my mistake of delaying the operation. This mistake I readily admit.

The more recent literature which could not be included in the papers previously mentioned, contains but few articles.

Schmidt reported the case of a patient who, years before, had been operated upon for carcinoma of the uterus. This patient developed symptoms suggesting calculus of the ureter. X-ray examination was negative. On catheterizing the ureter, an obstruction was met with. When contrast material was injected, the patient complained of pain in the leg. The contrast material was then found outside of the ureter. Because a metastasis of the tumor was suspected, operation was performed. A ureteral calculus was found.

Bach-Egan treated a 39 year old woman doctor who complained of right-sided colicky pains, and whose urine contained red blood cells and white blood cells. X-ray examination showed a distinct shadow of a calculus, strikingly unusual on account of its nearly mesial position. Cystoscopy showed purulent discharge from the ureter. In the wall of the bladder, laterally and above the ureteral orifice, a bulge was found which was half the size of a walnut. When the ureter was catheterized, no obstruction was met with. Retrograde pyelogram showed the shadow five centimeters mesial to the shadow of the ureter calculus. The catheter, which discharged clear urine was left indwelling, but this led to elevations in temperature. The bulging area of the bladder was then cauterized. A few days later, the scab came off, and a urate stone, the size of a pea, was passed. Complete recovery ensued.

Bäcker reported a case of pyonephrosis. Perforation of the ureter occurred and resulted in an abscess which followed the psoas muscle and reached Poupart's ligament. Nephro-ureterectomy and drainage of the abscess were done, and complete recovery followed.

Freshman reported the case of an elderly man. The patient had had vasectomy and prostatectomy. Some time after the operation, he suddenly developed pains in the region of the kidney and subsequently a swelling in the inguinal region. X-ray examination showed a shadow in the region of the second lumbar transverse process. Because perinephritic

extravasation of urine was suspected, operation was done. A huge cavity full of foul-smelling urine was found. The cavity reached from the kidney down to Poupart's ligament. Following drainage, the patient was cured. X-ray examination readily showed the calculus to be situated further caudally. Catheterization of the ureter met with no obstruction.

Goidin's case was a patient who had had attacks of colic for years. A shadow situated between the third and fourth lumbar vertebrae was found. Intravenous pyelogram showed no excretion of the dye on the affected side. Operation revealed an abscess cavity, which contained, besides urine and pus, also the calculus. There was a transverse rupture of the ureter. The kidney was full of abscesses. Extirpation was done.

If we consider our case in the light of reviewed literature, we find the following peculiarities: our failure to find the calculus, the rapid, though partly transient formation of calculi, rupture of the ureter discovered only by X-ray studies, and the relatively favorable outcome after many vicissitudes.

It is hard to make a prediction regarding the future health of the patient. Until the present time those calculi which were found retroperitoneally, in the retrovesical tissues, have remained quiescent. It is not altogether impossible that the fistula at some future time may discharge all the calculi of the ureter stump, and perhaps even those calculi which are now situated extraureterally. Such an event would mean the final healing of the fistula. Rupture of the chronic abscess into such surrounding organs as the bladder or rectum seems hardly probable. Rupture would be more likely to occur at the site of least resistance, viz., the old fistula.

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OPERATIVE TREATMENT FOR URETERAL STRICTURE DUE TO BILHARZIA

WITH A CASE REPORT

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In South Africa, particularly in the North Western Transvaal and Natal, there is extensive infestation with the Bilharzia (Schistosoma) haematobium, with the result that a urologist practising in these areas sees the end results of the disease very frequently. Up to the present there are no officially recognized findings that will lead one to proclaim a patient cured of the infestation. It is usually assumed that when no ova can be found in the urine on repeated examinations and when the patient has a normal eosinophilic count the patient is cured. This assumption I have repeatedly found to be incorrect for many of these patients still have visible Bilharzial lesions in the bladder and may have a recurrence of the Bilharzia without having been re-exposed to infestation.

The result of this state of affairs is that many years (ten to fifteen) after the original infestation and treatment these patients come to a urologist on account of repeated attacks of renal colic with no evidence of renal calculus. On cystoscopic examination one frequently finds the bladder mucosa to be almost completely avascular with only a slight depression on the ureteral ridge indicating the site of the ureteral orifice. Sometimes sandy patches are still visible and occasionally other traces of vesical Bilharzia can be seen. Ureteral catheterization is not infrequently quite impossible, although occasionally one can pass a very fine whalebone filiform through the orifice and so temporarily give relief from these repeated attacks of renal colic. It becomes necessary therefore to operate on these individuals to relieve the obstruction at the intramural portion of the ureter.

The following case is a typical example:

History. J. M., aged 22 years, male, was first seen March 23, 1936 complaining of repeated attacks of renal colic. He gave a history of having been exposed to Bilharzia ten years previously but had no recollection of ever having had the disease or of having had any terminal haematuria. Early in 1935 he had a very severe attack of right-sided renal colic radiating to the groin. The attack was accompanied by nausea and vomiting and lasted for six hours. Soon afterwards a similar attack occurred on the left side. At first these attacks recurred once in two or three months but recently they occurred once every week or fortnight.

With these attacks there were no urinary symptoms in the form of frequency, urgency or dysuria.   He had occasional headaches, his appetite had been poor for the two or three months previous to admission and his bowels were constipated.

Examination.   The patient was a tall, thin, pale youth.   The tongue was moist; heart and lungs, normal; abdomen, flat and soft.   The lower

FIG. 1. Uroselectan pyelogram showing typical Bilharzial ureteritis. The calyces and pelves are normal. Very slight dilatation of the upper two-thirds of each ureter. Advanced dilatation and elongation in the form of tortuosity of the pelvic portion; this is more marked on the left side than on the right.

poles of both kidneys were readily felt.   There was slight costovertebral angle tenderness on the left side but none on the right.

Cystoscopic examination on March 24, 1936 showed the bladder mucosa to be pale and avascular.   There were a few round white masses characteristic of infestation with Bilharzia scattered over the base of the bladder. No sandy patches were seen.   The right ureteral orifice was pinpoint, the left was not visible but now and again there was a tendency to ballooning at the site where the orifice should have been.   No indigo-carmine was seen even at the end of half an hour.

The bladder urine was clear, acid in reaction and contained no albumen, sugar, pus or organisms, nor were any ova detected. The eosinophil count was 2 per cent.

X-ray examination (Fig. 1) revealed no evidence of urinary calculi and after intravenous uroselectan we saw the calyces normally outlined. They were clear cut and showed no evidence of dilatation. The pelves were also within normal limits. The upper two-thirds of both ureters were slightly but uniformly dilated. The distal third showed the marked

FIG. 2. Uroselectan pyelogram of the same patient five months after operation, showing a definite return to normal. The dilatation and elongation of the pelvic portion of the ureters is definitely decreased.

dilatation and tortuosity which, when contrasted with the remainder of the system, made it typical of the ureteritis so characteristic of Bilharziasis.

A cystoscopic examination was performed on March 24, 1936. With a little difficulty a whalebone filiform was passed through the right ureteral orifice. This was followed by a second. On the left side it was not possible to pass even this fine instrument. Consequently the ballooning area at the site of the left ureteral orifice was burnt with a fulgerating electrode in the hope of perforating through into the ureteral lumen. The patient

had immediate relief of symptoms but was advised to be operated upon for the relief of the obstruction. This advice was accepted and the operation was performed April 28, 1936 using a technique which I have found to give very satisfactory results.

Operation. Through a low mid-line suprapubic incision the bladder was exposed and the peritoneum reflected off it on both sides to expose the ureters retroperitoneally. The ureters were found to be large, tortuous and very much thickened. A longitudinal ureterotomy incision was
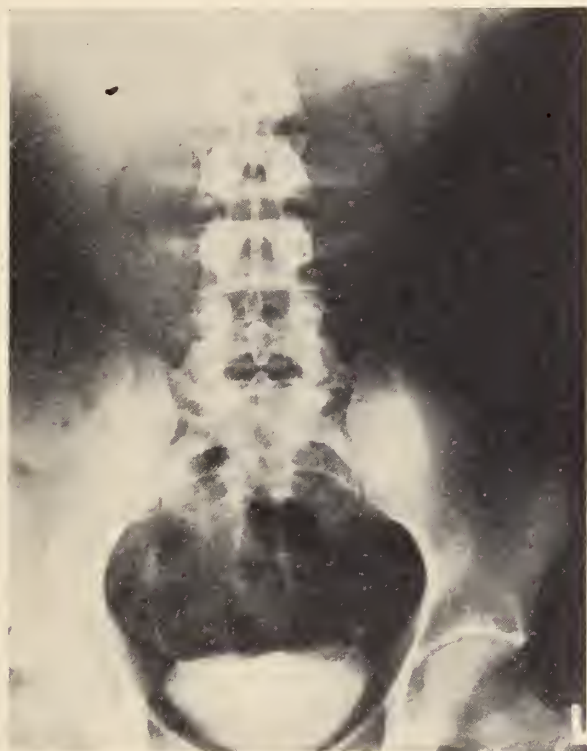
Fig. 3. Uroselectan of the same patient made a year after the picture shown in Fig. 2 (one year and five months after operation). Note that the pelvic portion of the ureters, as well as the remainder of the upper urinary tract, has practically returned to normal.

made in each ureter cutting through the thickened wall which was infiltrated with ova and with small areas of calcification. Through these ureterotomy openings it was, after some difficulty, found possible to pass a filiform guide through into the bladder. The bladder was then opened and under vision the steel follower passed down the ureter until its tip projected into the bladder. A V-shaped piece of intramural ureter and bladder was then excised. The ureteral and bladder mucosa were sutured together with #000 plain catgut so as to control bleeding and leave a wide ureteral orifice. A piece of rubber tubing about size 21 F. was then

passed through the new ureteral meatus up to and beyond the ureterotomy incision which was closed with ✳000 plain catgut. A similar procedure was carried out on the other side. Both these tubes as well as a separate tube in the bladder were allowed to come out through the suprapubic opening in the bladder and the abdominal wound was closed around them. A rubber sheath drain was placed on either side of the bladder to the region of the ureterotomy.

Course. By May 19, 1936, the patient had made a complete recovery, was dry and had left the hospital. He had had two full courses of Fouadin injections before operation and two more after the operation was performed.

When seen on September 7, 1936, the patient had had no further attacks of colic and was free from symptoms. On cystoscopy the bladder appeared to be normal and there was no further evidence of Bilharzia except for the pallor of the mucosa. Both ureteral orifices were widely patent and readily admitted ✳9 F ureteral catheters. A bilateral urogram (Fig. 2) showed a great deal of improvement with normal emptying.

On April 10, 1937 (a year after the operation), the patient reported that he was having some pain on the left side. His ureter was very easily dilated and the next day he passed a small ureteral calculus.

On August 23, 1937, the patient was still free from symptoms. The urine was sterile and contained no albumen, sugar, pus nor ova but was cloudy with amorphous phosphates, the pH being 8.0. Uroselectan pyelogram (Fig. 3) showed the urinary tract to be perfectly normal on the right side while on the left side there was very slight deformity in the distal third to show that there had once been some disease.

COMMENT

Infestation with the Bilharzia haematobium results in most instances in a deposition of ova in the various pelvic organs especially in the lower ends of the ureters and the bladder. As has been shown, the infected ureter readily dilates even with no actual mechanical obstruction. Later, as a result of the scar formed to encapsulate the ova, the intramural portion of the ureter becomes more and more occluded. Accompanying this there is a more rapid dilatation and also elongation of the diseased portion of the ureter. The result is, as one so frequently sees, dilatation and tortuosity of the distal portion of the ureter with the upper portion of the ureter, the pelvis and calyces remaining normal. With persistence of the obstruction at the uretero-vesical valve, the upper portion of the ureter, the pelvis and calyces will naturally also dilate. Fortunately before this happens the patients usually seek medical aid for relief from their attacks of renal colic.

The method of treatment as described in the case reported above has been found, in my experience, in a large series of cases, to be the most efficient.

PERFORATION OF A PERINEPHRITIC ABSCESS INTO THE STOMACH*

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Perinephritic abscesses which develop in the course of an infection of the kidney or seemingly by metastasis without any intermediary infectious kidney lesion, perforate in accordance with their location. At times this takes place through weak points in the musculature of the lumbar region, such as the foramen Leshafti, thus coming to lie underneath the skin of the lumbar region. Perforation may also take place through the diaphragm into the pleural cavity and even through the lung tissue into the bronchi. Again, burrowing along the psoas muscle, they may perforate into one of the hollow organs of the pelvis, rectum, uterus or bladder. If the perinephritic abscess develops ventral to the kidney—a condition rather rare because of the small amount of epi- and perirenal fat at the ventral aspect of the kidney—it is possible for such a "prerenal" abscess to perforate through the peritoneum into the abdominal cavity as well as into its organs. Perforation into the peritoneal cavity, which leads nearly always to a fatal diffuse peritonitis, is rather rare. The perforation is commonly so slow in its occurrence that intraperitoneal adhesions are formed in time at the site of the perforation and serve to prevent the pus from invading the free abdominal cavity. The perforation thus remains "covered." Prerenal suppurations perforate with greater frequency abdominal organs, such as the colon, and especially the descending colon. Of much rarer occurrence is a perforation of a perinephritic abscess into the small intestine. Perforation of a perinephritic abscess into the stomach may also occur, as will be shown by the following observation, which is reported because of the rarity of such an occurrence.

CASE REPORT

A housewife, 34 years of age, was referred to us for treatment of a chronic pyuria and transient severe pains in the left lumbar region accompanied by high temperature. She had had scarlet fever, measles and diphtheria in her childhood; otherwise she had remained well until the age of 28. At that time she became married and shortly after her marriage developed signs of a pyelonephritis accompanied by the frequent occurrence of severe pains in the left lumbar region, and long periods of elevated temperature.

* Translated from the German by Dr. Leo Moschkowitz.

Because of that the patient was confined to bed for periods of months. In the course of her illness the patient was frequently advised by her physicians to undergo an operation on the left kidney, which was always refused. The patient frequently changed her medical advisers and consulted more than thirty physicians during a period of seven years. A few months before she came under my observation, she passed through a period of illness with high fever, severe nausea, frequent vomiting and pronounced pains in the left kidney region. The vomited matter was said to have consisted of mucus-like material and only once had there been noted purulent masses in the vomitus. The patient noticed during the later months a tumor formation in the left epigastrium which varied in size from time to time. As the swelling periodically increased in size, the patient felt worse. For that reason she finally decided to consider operative interference.

Examination. The patient was a pale, emaciated, very nervous woman. The heart and lungs were normal. The left kidney was markedly enlarged, not movable either on palpation or on respiration. It was slightly tender. The right kidney was not palpable. The abdomen was slightly distended. The urine was very purulent, containing $\frac{1}{8}$ per cent albumin with no casts or sugar. The sediment contained much pus, no red blood cells, but numerous B. coli. Cystoscopy revealed a normal bladder and a normal orifice of the right ureter; there was efficacious excretion of indigo after nine minutes on the right side. The urine of the right kidney contained albumin but no pus. The urine of the left kidney was thickly purulent; there was complete absence of indigo excretion on the left side. The vaginal examination was negative; the ureter was not infiltrated. Sedimentation time of the blood was 12 mm. at the end of the first hour. The blood examination showed only a low grade anemia. Roentgen-ray examination revealed a marked shadow in the region of the left hypochondrium; no stone formation in the region of the kidney.

Operation. A left sided nephrectomy was performed under ether anesthesia on May 4, 1935. At the beginning of the anesthesia, even before the patient was moved from her bed to the operating table, she vomited large quantities of very foul smelling, purulent material which was very suggestive of a bacillus coli pus. This indicated the probability that the vomiting reflex which was initiated early in the anesthesia, pus from the kidney and from the perinephritic abscesses emptied itself into the stomach. The conjecture was verified after the disclosure of a left-sided pyonephrosis. Each pressure on the kidney which was distended with urine and pus, caused the discharge of purulent urinous material from the mouth of the sleeping patient. During further dissection of the kidney a prerenal abscess cavity with a firm wall was found. It communicated with the markedly dilated renal pelvis as well as, by means of a thin, tortuous fistular canal, with the cardia of the stomach. The fistular canal was

surrounded by dense, fibrous adhesions. The exposure of the site of perforation in the stomach was possible without opening the free peritoneal cavity. The resection of the kidney pole from the spleen caused only a small peritoneal tear, which was closed immediately with a catgut suture. After removal of the suppurated kidney the site of perforation in the wall of the stomach could be ligated and completely closed by suturing over it the surrounding fibrous adhesions. The lumbar incision was partly closed and partly packed. The histological examination of the removed kidney showed advanced shrinkage of the renal tissue with degeneration of still existing glomeruli; only a few tubules were present and these were in the main narrow, some being dilated and filled with hyaline casts. In the wide interstitial renal tissue there were diffuse and dense infiltrations of lymphocytes, eosinophiles and plasma cells. The mucous lining of the renal pelvis was destroyed and replaced by densely infiltrating granulation tissue. There were also extensive hemorrhages in the wall. The histological diagnosis was hydronephrotic contracted kidney with pyelonephritis.

Postoperative Course. Recovery took place in the course of three weeks. The urine cleared rapidly. Her temperature remained normal after the operation and the patient remained well and free of any gastric disturbances.

COMMENT

Observations on similar conditions are apparently rare; at least they have seldom been reported. In his monograph Hilgenreicher stated that only eight instances of this condition are found in the literature. They are instances in which the renal pelvis or kidney are connected by a fistula with the stomach. All these fistulae were the result of a perforation of a prerenal abscess into the stomach. In only one case was it caused by perforation of an echinococcus cyst. In addition to the cases cited above, there is only one other case described by Nichols. Since 1898 no new contributions to the subject of perforation of perinephritic abscess into the stomach have been made. The explanation why such observations are not reported is to be found in the fact that perinephritic abscesses nowadays are opened much earlier than previously; thus, serious complications, such as perforation into the stomach, are prevented. The condition becomes a rarity; for it takes time for the destructive process to find its way through the thick, muscular wall of the stomach. A perforation of the colon occurs much more rapidly and that is the reason why the occurrence of such perforations is still quite frequent. From a study of the cases reported in the literature it appears that the recognition of a fistula between kidney basin and stomach is relatively easy. Patients suffering from such fistulae occasionally vomit purulent uriniferous material. In other cases, as for instance in the case described by von Melion, they may

discharge with their urine undigested food particles. In my patient the diagnosis of renal pelvis—stomach fistula was made immediately before operation because the patient vomited uriniferous purulent material in the early stage of the anesthesia. In giving her history the patient had mentioned the fact that she had vomited foul smelling material. This statement, however, was not interpreted correctly because the vomited matter was seen only by the patient herself and not by a physician or otherwise qualified observer. The statement of this rather nervous patient was not considered to be reliable. The diagnosis of renal pelvis—stomach fistula was then only made when the patient, in the first stage of anesthesia, vomited large quantities of foul smelling, purulent material as though it contained B. coli. This diagnosis was further substantiated after the kidney was exposed. At that time pressure upon the suppurated kidney caused discharge of pus from the mouth.

Nowadays, such a case as this is not of great significance. It is mainly a curiosity. Nevertheless, it teaches a lesson,—that a patient suffering with a perinephritic abscess may be cured completely, even if some grave complication, such as perforation into the stomach, has occurred.

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A POINT IN THE CLINICAL DIAGNOSIS OF
URETERAL CALCULUS

A PRELIMINARY REPORT

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Some years ago I made the observation that in certain cases of calculus in the lower third of the ureter, that is, below the brim of the bony pelvis, there was one point in the abdomen where tenderness was more marked than elsewhere. After further observation it was found that this point, whether on the right or on the left side, was located just below the one described by McBurney (1) as being the site of maximum tenderness in acute appendicitis. McBurney described this point in the adult as "one and a half to two inches inside of the . . . anterior superior spinous process of the ilium on a line drawn to the umbilicus." He also remarked that it was "not enough to compress with the whole hand the region of the iliac fossa" but that pressure must be made with the finger-tip "to determine that the most sensitive point is a definite one in most cases."

In just such a manner the writer has located the point of maximum tenderness to be described. It can be found with great accuracy by first locating McBurney's point. One then moves the finger-tip downward and inward one inch from this point and in a direction at right angles to the line on which McBurney's point lies (Fig. I). By pressure with the finger-tip the patient will show evidences of very definite pain, sometimes even with only moderate digital pressure. There is generally no spasm unless deep and vigorous pressure is made. As in McBurney's observation, it is not enough to press with the entire hand over this area, as, while there may be more or less tenderness, there may be none at all, unless digital pressure is used. In no instance has there been evidence that hyperaesthesia of the skin is a factor. Having located this point, on one side or the other, concentric circles can be drawn around it, as shown in the diagram. In a typical and well-marked case finger-tip pressure around the most distant circle may elicit no tenderness; as the finger moves from one circle to the other toward the center tenderness becomes more and more marked, until its maximum is found to be at the point indicated.

The phenomenon has now been looked for in one hundred and fifteen cases of proved ureteral calculus. Positive findings were obtained in

forty-seven, or 40.8 per cent, some on the left side, some on the right, and about equally divided between men and women. Probably in a majority of these cases the ureter was no more than slightly or moderately dilated, nor was infection of any great severity present in more than a few. It did not seem to make any difference in the findings whether the stones were single or multiple, large or small, or whether they lay just outside of the bladder or just below the bifurcation of the iliac vessels. In a few instances it was found that after the removal of the stone, either by spontaneous passage or by operation, the tender spot could no longer be demonstrated. McBurney stated that in acute appendicitis "from the first
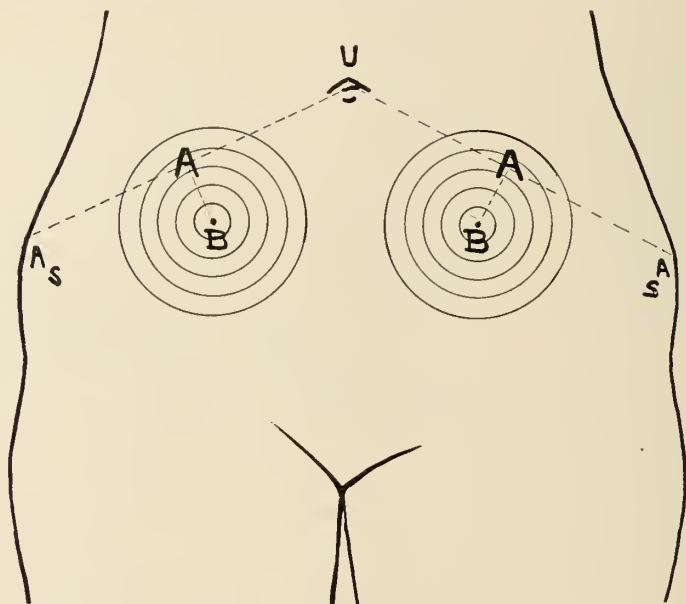
Fig. 1. Umbilicus, U; Anterior Superior Spine, AS; McBurney's point, A; Barney's point, B. Concentric circles indicate intensity of tenderness as one approaches or leaves the point B.

hours of the disease even up to the end of several days, this sign may be clearly made out in every case." The writer acknowledges that he has no evidence as to how long this tenderness may persist in the presence of a stone, nor does he claim that it is present in "every case." The observation is described for what it may be worth, and in the belief that it may, in certain cases, help to clear up an obscure diagnosis. It is known that about 4 or 5 per cent of stones in the lower third of the ureter cannot be demonstrated by X-ray examination, either because the stone is composed of uric acid, or because it has the same density as the sacrum against which it lies. In these cases the diagnosis would doubtless eventually be made by cystoscopic study and by the passage of a wax-tipped catheter.

A case related to me by my colleague, Dr. Edward L. Young, Jr., illustrates some of the observations made in this communication. The patient, a man of 40, without previous urinary or abdominal symptoms, was seized with sudden, severe pain in the right lower quadrant. There were no urinary symptoms, but there was nausea. Temperature was 99.2°F.; white blood count 23,000. Urine sediment showed an occasional white cell, no red cells. Marked tenderness but no spasm (until deep pressure was made) was found on the right at the point which I have described. There was no costo-vertebral tenderness. In the belief that this was a case of acute appendicitis, preparations were made for operation. During this time and on the chance that this case might be one of ureteral calculus, cystoscopy was done. A small stone was seen protruding from the right ureteral orifice. The stone was removed by rongeur forceps. The pain disappeared almost at once and the tenderness subsided by the time the patient returned to his bed. There were no further symptoms.

When it comes to affording an explanation of this point of tenderness, the writer finds himself rather helpless. Certain observations made on the ureter at various times, while of interest, do not seem to throw much light on the question. Some years ago I had the privilege of seeing an old lady on another service at the Massachusetts General Hospital who had had both ureters brought out on the back just below the costo-vertebral angles. About two inches of normal-looking ureter protruded beyond the skin on either side. The ends of these ureters could be snipped with scissors or crushed with a clamp without causing any sensation to the patient. Nor did she realize it when a crochet needle was inserted in the ureter and moved vigorously up and down in the lumen, producing considerable bleeding by trauma of the hook. When, however, a small clamp was inserted into the ureter and then opened, thereby dilating its lumen, quite severe renal colic was produced, subsiding promptly when the tension was released. From these observations it may be deduced that renal or ureteral colic is produced, not by the roughness of a stone, but by the dilatation of the ureter or renal pelvis which it causes.

More recently, and inspired by the work of my colleague, Dr. Chester M. Jones of the Medical Department of the Massachusetts General Hospital, I tried the effect of dilatation of the intact ureter. A Dourmashkin catheter was passed up the ureter, first on one side and then on the other, in three female patients. In two both ureters were normal, in one there was considerable dilatation on one side, none on the other. The bag surrounding the tip of the catheter was dilated to what appeared to be its maximum size (using about 2 c.c. of 12 per cent sodium iodide solution) when the catheter was in the ureter at 25, 20, 15, 10 and 5 cm. A series of X-ray examinations in one of these patients showed that the bag was dilated laterally and that it had not been merely elongated in the lumen of the ureter. Two of the women had no pain or tenderness at any

time or in any place when the bag was dilated. The third patient experienced a little momentary pain in her normal left ureter when the bag was dilated at about 10 cm., but there was no tenderness. This experiment with the ureter has therefore failed thus far in producing pain and tenderness from the ureter which Jones was able to elicit by the inflation of a bag at various points in the gastro-intestinal tract

I also tried to get help from the post mortem table. In two bodies, long, sharp and rather heavy steel pins were driven through the abdominal wall on either side at the point under discussion, until they were fast in the bone. The abdomen was then opened, care being taken not to dislodge the pins. On exposing the ureters by dissection of the retroperitoneum and without disturbing their position, they were found in both instances to lie almost an inch to the medial side of the pins. It would therefore seem as if pressure with the finger-tip does not compress either the ureter or the stone lying within it. It undoubtedly does impinge upon both layers of the peritoneum, upon the coils of gut lying beneath and upon the muscles of the abdominal wall and of the pelvis. That none of these structures is the seat of pain is obvious from the fact that in the absence of stones and even in the presence of 60 per cent of stones the phenomenon is non-existent.

The work of various investigators has shown that the ureter is very richly supplied and in a most intricate manner by the sympathetic nervous system. The recent works of Wharton (2) to which the reader is referred for details, has shown that the ureter is supplied by nerves from the lowest renal ganglion at the head of the spermatic and ovarian plexuses and from the aortic, hypogastric and pelvic plexuses. Not only this, but it is in close contact with "the rich network of fine nerves which course through and directly beneath the peritoneum. . . ." Wharton has shown first, that these nerves can be divided without interfering with ureteral function, and, second, that, clinically, the patient is relieved of ureteral colic. This is "rather strong evidence," Wharton says, "that at least one of the functions of these nerves is to convey sensations of pain—in other words that they contain afferent or sensory fibres."

It is probable that further prosecution of the work carried out so beautifully and painstakingly by Wharton will throw light on the problem which I have presented.

In the present state of our knowledge it is not clear why the point of tenderness under discussion is situated where it is, or why it is not present in all cases. Neither does it explain why, if it is absent at the point described, it is not likely to be present elsewhere. Possibly these variations indicate that the location or arrangement of the ureteral sympathetic nerve supply varies with different individuals, thus accounting for the discrepancies observed.

Further observations, both clinical and experimental, may help to clarify this problem.   There is no doubt that any procedure or observation which will aid in the resolution of a difficult and obscure diagnosis is worth while.

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ROENTGENOGRAPHIC DATA IN ASSOCIATION WITH RENAL DISEASE*

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A careful, detailed study of the preliminary roentgenogram, glibly referred to as the "flat plate," often will reveal many data which are easily overlooked. The specialist is likely to look only for evidence of lesions in his individual field and to disregard roentgenographic data indicative of lesions which may be of equal clinical importance in fields other than his own. Although the urologist, particularly if he practices alone, is a frequent offender in this respect, he is not so likely to err if he has had a wide general training prior to specialization and if he maintains his interest in the general fields. He is still more fortunate if he is closely associated with a group of men with whom he coöperates in general examination of the patient and, as a result, keeps in touch with a broad clinical interpretation and abreast of advance in various fields.

The question often has been asked whether urographic interpretation should be made by the roentgenologist or the specialist in the field concerned. Much depends on the experience of the interpreter in the field concerned and on his intelligence. As a general rule, the clinician skilled in roentgenographic interpretation in his field can read some things in the roentgenogram which may often be insignificant to one who is without clinical knowledge. On the other hand, wide familiarity with roentgenography in various fields of medicine permits the experienced roentgenologist to recognize lesions which might easily be overlooked. It would be well for the urologist, therefore, to familiarize himself with general roentgenographic interpretation and to be continually on the lookout for evidence of lesions in fields other than his own.

HELPFUL AND CONFUSING SHADOWS

The vertebrae and pelvic bones. Interpretation of the preliminary roentgenogram frequently will offer evidence which may have direct bearing on recognition of various types of urologic disease. In the long list of lesions the following conditions may be noted and always should be looked for: 1. There may appear evidence of disease of the vertebrae, such as lipping of the vertebrae and deformity of the spinal processes; these often occur as results of spinal arthritis. This condition is often

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the cause of pain which may be easily confused with pain of renal origin. 2. Destruction of vertebrae as a result of old tuberculosis, when present, together with other roentgenographic evidence of tuberculosis of the genito-urinary tract, is of corroboratory value. 3. Spina bifida occulta always should be looked for when the symptoms are those of urinary difficulty or incontinence. My impression is, however, that the importance of spina bifida occulta of slight degree is sometimes exaggerated, since the condition is often observed unaccompanied by evidence of a lesion in the urinary tract. However, when deformity of the sacral vertebrae is great, vesical innervation is frequently impaired. 4. A deformity often noticed in the original film involves the last two lumbar and the first sacral vertebrae and is characterized by apparent fusion of the vertebrae, together with accentuation of the shadows. This condition is described by the term "spondylolisthesis" and its clinical importance has been recognized only in recent years. In order to appreciate the deformity more clearly, it is usually advisable to make a lateral roentgenogram, which will bring out more clearly than the anteroposterior roentgenogram the dislocation and over-riding of the vertebrae. Although spondylolisthesis occurs rather commonly, it may not cause symptoms. In some cases it is the cause of pain without involving the urinary tract. In a few cases, however, the spondylolisthesis, with resulting spinal pressure, will cause marked disturbance of innervation of the bladder, with resulting neurogenous, or cord, bladder. 5. Variable opaque areas frequently are seen in the various pelvic bones or vertebrae. They may be difficult to interpret and in some cases are suggestive of metastasis. Roentgenographic differential diagnosis of osseous lesions caused by metastasis, Paget's disease, fibrosis and sclerosis may be difficult. Indefinite changes which may be localized or scattered throughout the pelvic bones are often observed and may be very confusing. In most cases these areas are of no clinical significance. That recognition of the nature of these shadows may be difficult is shown by the variable interpretation which may be given them by different roentgenologists.

Scoliosis and other displacements. A variable degree of vertebral scoliosis is frequently observed in the roentgenogram. This may be acute and accompanied by destruction of the vertebrae, such as frequently is seen in association with tuberculous spondylitis. Extreme scoliosis may be the cause of renal displacement, although rarely does ureteral obstruction result. Minor degrees of scoliosis often observed in the routine roentgenogram may be postural and this possibility must always be considered and verified. When persistent, however, minor degrees of scoliosis may be of considerable diagnostic importance and can be caused by a variety of lesions. They may be the result of spastic conditions, hypertrophy, atrophy, or deformity of the vertebrae. Beer and others have called attention to the importance of scoliosis in recognition of renal lesions

such as acute perinephritis (fig. 1). Persistence of scoliosis in repeated films should be of definite clinical importance to the urologist if corroboratory clinical and urographic evidence of renal disease is also present. On the other hand, the absence of scoliosis does not necessarily exclude a renal lesion (fig. 2). Scoliosis may be observed in association with a variety of acute and chronic lesions in the thorax as well as in the kidney, as has been pointed out by various observers.

Rigler and Manson (4) regarded upward displacement of the diaphragm and evidence of displacement of the colon as more important than either

Fig. 1. Scoliosis and obliteration of the psoas muscle and right perinephritic abscess.

scoliosis or obliteration of the psoas shadow. This was not corroborated by Shane and Harris. Cabot referred to fixation of the kidney in cases of perinephritis when the patient is placed in the dorsal or in the Trendelenburg position.

Visceral calcification. It is well known that many shadows in the roentgenogram are caused by calcification of renal and ureteral tissues and not by urinary lithiasis. Without considering the subject at length, the more common sources of error may be mentioned. Confusion of shadows cast by gallstones and by renal stones is a frequent cause of misinterpretation.

Although the shadows of a gallstone and of a renal stone usually differ markedly, nevertheless the two may be similar in contour, structure, density and position.   Laminated renal stones are frequently present, while gallstones often will cast a uniform, dense shadow suggestive of renal lithiasis.   The position of the shadow does not necessarily identify it, since renal shadows are seen as high as the tenth intercostal space and gallstones may be as low as the crest of the ilium.   In doubtful cases the shadow usually can be identified by urography.

FIG. 2. No scoliosis, but enlargement of the left renal shadow

Median shadows. Shadows which appear close to the spine, or in the midline, may be misleading when the possibility of renal malposition or renal fusion is forgotten.   In fact, since lithiasis so frequently occurs in the fused kidney, the possibility that this anomaly is present always should be considered in the presence of median shadows.   Calcification of the pelvic organs of the female sometimes is confusing and requires urographic interpretation.   This condition is easily confused with calcified lymph nodes and with phleboliths and areas of calcification in the various pelvic organs.   Shadows caused by prostatic stone frequently are overlooked.   In the first place, the pubic region is frequently out of focus in

the films and is not clearly visualized. Again, shadows caused by prostatic stone are variable in position, depending on the angle at which the exposure is made. They can be observed several centimeters below the pubic bone, behind the pubic bone, or as high as 4 or 5 cm. above it. The shadows themselves may be minute and indistinct and may escape detection unless carefully observed. Stone in the male urethra is easily overlooked, since the urethra, and particularly the membranous and anterior urethra, is so often out of the usual roentgenographic focus.

The psoas shadow. The importance of careful inspection of the outline of the psoas muscle in the roentgenogram is not generally appreciated. It is true that in the course of routine roentgenographic examination various technical factors may cause obliteration of this outline. The obliteration is usually bilateral or is easily recognized as being attributable to a faulty film. When the outline of the psoas muscle on only one side fails to appear in repeated films, however, it usually becomes of definite clinical importance. The finding is probably of greatest clinical significance in diagnosing perinephritic abscess. Although obliteration of the shadow of the psoas muscle is not pathognomonic of perinephritic abscess, and although it may occur with other renal lesions, the obliteration usually is localized to the renal region and the shadow of the entire psoas muscle does not disappear.

THE RENAL SHADOW

Careful inspection of the outline of the kidney in the original roentgenogram is often of much clinical value. Unfortunately, the renal outline is not always clearly defined in the roentgenogram and can be easily confused with that of adjacent organs and tissues. In addition, the outline of adjacent tissues may simulate that of the kidney exactly and identification may be impossible. On repeating the roentgenogram the following day, however, more exact interpretation often becomes possible. On several occasions I have observed what appeared to be a typical renal shadow in the roentgenogram of a patient, one of whose kidneys had been removed or was absent. It is often difficult to determine the exact outline or limits of the kidney because of overlying intestinal shadows. An apparently enlarged or irregular kidney may, in subsequent roentgenograms, prove to be practically normal in size or contour. Nevertheless, recognizing the possibility of error, careful examination of the renal outline often is of much value.

Variations in size. Although the outlines of the two kidneys, when normal, usually are similar and symmetrical, variations in size and contour of the kidney are sometimes observed when there is no clinical evidence of disease. Nevertheless, a striking unilateral increase in size should call attention to the possibility of a renal lesion. In such cases careful study of the smaller kidney always should be made because evidence of a current

or previous lesion often can be determined. When one kidney is markedly enlarged and the renal shadow on the other side is absent, the possibility of agenesia must be considered. As I have described previously, unilateral renal hypertrophy, with agenesia of the other kidney, usually is accompanied by renal ptosis and inspection of the shadow of the psoas muscles often discloses comparative atrophy on the side of the absent kidney (figs. 3 and 4). Although the size of the renal outline usually is commensurate with that of the patient, nevertheless marked variation

FIG. 3. Right agenesia with obliteration of right psoas muscle. Outline of left kidney enlarged, with ptosis (grade 2).

sometimes will occur. When the outlines of both kidneys of a patient of average size are unusually large, the cause should be ascertained. Abnormal increase as well as abnormal decrease in size sometimes is observed in different forms of nephritis. The possibility of polycystic kidney also must be considered, particularly if the renal outline is irregular. The fat which envelops the kidneys of adipose individuals frequently exaggerates their size. For this reason, the renal outline of fat individuals is often visualized much better than is that of the average patient. Unilateral increase in the renal outline frequently is seen accompanying an

obstructing ureteral stone. Its temporary nature, probably as the result of congestion, is demonstrated by the return to normal after the stone has been removed.

Abnormal decrease in size of both kidneys, not explained by the size of the patient, may also indicate disease, as suggested in an earlier paragraph. Unusually small renal outlines, however, often are observed without its being possible to demonstrate any definite evidence of pathologic change or disturbance of renal function. However, when there is unilateral decrease in size of the renal outline in repeated films, atrophy,

Fig. 4. Right agenesia with widening of psoas muscle as occasionally observed. Left kidney is greatly enlarged with ptosis (grade 1).

as the result of various factors, may be inferred. If evidence of renal infection is absent on culture, or if the urographic outline is abnormal, the possibility of congenital hypoplasia must be considered.

Irregularity in outline. Although irregularity in the renal outline sometimes is apparent rather than real, and is caused by intervention of overlying tissues, it may be of considerable importance in clinical interpretation.

Irregularity in outline, accompanied by increase in size, often is suggestive of neoplasm or renal cyst. This is particularly true when the irregularity or increase in size is localized to either pole. Irregularity in the outline of the kidney, particularly of the middle portion, frequently

is observed when no evidence of a renal lesion can be found on urographic or cystoscopic study. It must be remembered, however, that both neoplasm and cyst at the distal end of the kidney may not cause deformity of the renal pelvis or calices. When the enlargement is in the middle portion of the kidney and there is little or no urographic deformity, the lesion is more likely to be of a cystic than of a neoplastic nature. It should also be remembered that when the irregularity is owing to a cyst, the shadow cast by the fluid in the cyst is denser than that caused by neoplastic tissue.

Renal displacement. The outline of a large, extrarenal tumor can be easily confused with that of the kidney. As a rule, differential diagnosis, and identification of the extrarenal tumor, can be made with the aid of urography.

The position of the renal shadow can vary widely without any apparent pathologic cause. In fact, congenital aberration in embryologic renal ascent gives the kidney a wide range in the position it may take. The outline of the right kidney is normally somewhat lower than that of the left. When the outline of the right kidney is higher than that of the left, there is usually some pathologic cause, although it may be congenital.

Among the various causes of renal displacement the following may be mentioned: congenital abnormality, extrarenal pressure and postoperative or inflammatory cicatrization. A fixed lateral position of one kidney, without urographic evidence of an intrarenal lesion, usually is the result of displacement by a median, extrarenal lesion. However, this condition can be observed when no such lesion is discovered, and may result from a congenital cause.

When the renal outline assumes a median position, the possibility of renal fusion or congenital dystopia must be considered. When the position of the kidney is caudad, it becomes necessary to distinguish between congenital renal dystopia, acquired dystopia, and displacement.

THE NEED OF CARE

The foregoing are only a few of the data which can be derived from the original roentgenogram, but they should suffice to emphasize the necessity of careful, detailed interpretation based on clinical experience.

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THE TREATMENT OF ABDOMINAL CRYPTORCHIDISM*

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There is now very general agreement among physicians of experience in the treatment of congenital misplacements of the testis that in all of the varieties, other than the abdominal type, surgical treatment is now very commonly required in order to obtain a satisfactory position for the testis. It is true that the place which will ultimately be held by the treatment by so-called hormones in helping to obtain a normal position of the testis is still undetermined. That it will frequently fail seems certain. That it will sometimes succeed has been apparently demonstrated, though one may remain skeptical as to whether many of the cases in which completely satisfactory results have been attained were not, in fact, cases of physiological cryptorchidism rather than true anatomical misplacement.

In contrast to the relatively fixed opinions in regard to the more common varieties of abnormality of position, there is still grave difference of opinion in regard to the proper management of those cases in which one or both testes are retained within the abdomen. Until relatively recent times, it has been commonly advised that they be left alone, less commonly suggested that, if the condition is unilateral, that testis should be removed. Without having undertaken an exhaustive survey of the more recent literature, one finds the following more or less characteristic opinions: Professor McCrea says that in abdominal cryptorchidism (unilateral), the testis "may, if feasible, be brought down into the scrotum, otherwise is best left in situ." If bilateral, he suggests bringing down one side and abandoning the other to its fate. Ainsworth-Davis says in substance that the treatment should be operative in all cases of imperfect migration other than abdominal in which the diagnosis is made over the age of five years. Pankratiew recommends replacement and fixation of the testis in the abdomen in cases where difficulty in bringing the organ down into the scrotum is met with. Counseller says replacement of the testis in the abdomen with section of the vas deferens or replacement between the transversalis fascia and the peritoneum, if the condition is bilateral, may be indicated in a small percentage of cases.

Such quotations could be considerably multiplied. Some surgeons even advise and practice orchidectomy when the condition is unilateral.

The reasoning upon which these conclusions are based does not appear to

me to be convincing. It would seem that if replacement in a strictly normal relation to the scrotum is sound for the other varieties of cryptorchidism, such reasons would be even more compelling in cases in which the testis is retained within the abdomen. This view is predicated upon the following premises: (1) The lesion is commonly bilateral and consequently the patient is inevitably or nearly inevitably sterile. (2) Though there is wide disagreement as to the increased danger of the development of cancer in the abnormally placed testes, there is practical unanimity in the opinion that cancer of the testis is importantly more common in the abnormally placed organ. I know of no convincing evidence tending to show whether the development of cancer is more common in the testis retained within the abdomen than it is in the other varieties of misplacement, but I think it safe to say that it is at least equally common. This consideration becomes more important for the patient whose testis is inaccessible to palpation within the abdomen. Modern thinking appears much in agreement with the view that the probability of cure of cancer of the testis depends upon relatively early diagnosis. Such early diagnosis is at least possible where the testis lies in a normal position and not impossible where the testis lies in the inguinal canal or in one of the rarer abnormal positions. On the other hand, early diagnosis of cancer of the misplaced testis retained within the abdomen is impossible. As a rule such patients are not seen until the occurrence of abdominal pain, metastasis, or general constitutional deterioration suggests abdominal exploration. This fact alone requires us to be more concerned in regard to the proper replacement of the testis in abdominal cryptorchidism than in any of the other varieties.

The reasons which lead to the suggestion that the testis should be left alone, anchored in some abnormal position, or even removed, are apparently based upon the assumption that the testis occupies so high a position that it cannot be safely and satisfactorily brought into a normal relation. This is true if it is expected to obtain sufficient lengthening of the cord to place the testis in the bottom of the scrotum at one operation. I propose here to submit evidence tending to show that by the use of a three stage procedure, satisfactory results can generally be obtained.

Without regard to the particular position occupied by the misplaced testis, it is sound doctrine to undertake replacement by surgical means between the ages of seven and ten. Few patients with true cryptorchidism will find that the testis descends into a wholly satisfactory position after that age. This, of course, is violently untrue in regard to the many patients with physiological cryptorchidism, and in them the migratory testis will frequently come permanently to rest in a normal position after the ages above suggested. Without at this time going into the distinction between true cryptorchidism and physiological cryptorchidism, it may

be suggested that the size and conformation of the scrotum is important in the diagnosis. In the true cryptorchid, the scrotum on one or both sides shows obvious lack of development for the corresponding age. On the other hand, in the physiological cryptorchid, the development of the scrotum may be quite normal and symmetrical in cases of unilateral failure of descent and, where the condition is bilateral, the scrotum may appear within normal limits and symmetrical.

PRINCIPLES INVOLVED IN THE MULTIPLE STAGE OPERATION

First stage. 1. The testis should be exposed by incision through the structures covering the inguinal canal as is done in the other types of misplacement. The incision should, however, be extended upward, dividing the fascia of the external oblique muscle for a considerable distance above the internal inguinal ring. The fibers of the internal oblique, which loop over the region of the internal ring, should be divided and the hernial sac, if one exists, should be freely opened on its anterior surface allowing satisfactory exploration of the abdomen (fig. 1). Careful freeing of the spermatic cord and the vas deferens is essential. Particular attention should be paid to the freeing of the spermatic cord from its attachment to the parietal peritoneum, and also, from its attachment to the retroperitoneal tissues for some distance above the level of the internal inguinal ring. In this way as much lengthening of the cord as is possible, having due regard to the vessels of the cord, should be obtained.

2. In freeing the testis from its peritoneal covering, which will ordinarily surround it completely in the cases of abdominal retention, a sufficient cuff of peritoneum should be left attached to the testis so as to allow the formation of a tunica vaginalis later in this stage of the operation.

3. The testis should now be drawn down to the lowest point which it will reach without producing improper tension upon the vessels or upon the vas. The flap of peritoneum which has been left attached to the testis should then be united over the surface of the testis in such a way as to create a tunica vaginalis. This having been accomplished, the testis should be anchored by suture, using some loose tissue, preferably in the region of the lower pole, to the posterior tissues of the inguinal canal. It will almost invariably be possible to bring the testis down to the level of the normal external inguinal ring. In some cases it can be brought to an even lower level without objectionable tension. It will sometimes be necessary to remove a certain amount of subcutaneous fatty tissue in the region of the spine of the pubis in order that coaptation of the tissues, particularly the fascial layers, over the testis may not bring pressure upon the organ.

4. The wound is then closed, bringing all of the layers together in front of the cord. This having been done, no further operation should be undertaken for at least a year and no objectionable consequences will result if a longer period elapses.

Second stage. 1. At this operation the wound should be reopened through the scar of the previous operation. The creation of an hydrocele sac, which is objectionable when the testis can be placed in the bottom of the scrotum, will be found greatly to facilitate the freeing of the testis from its abnormal bed, since it will have become adherent to the tissues only posteriorly.

2. The dissection of the cord must be repeated, the incision being carried above the level of the internal inguinal ring and the cord redetached from its relation to the parietal peritoneum and the tissues of the retroperitoneal space.
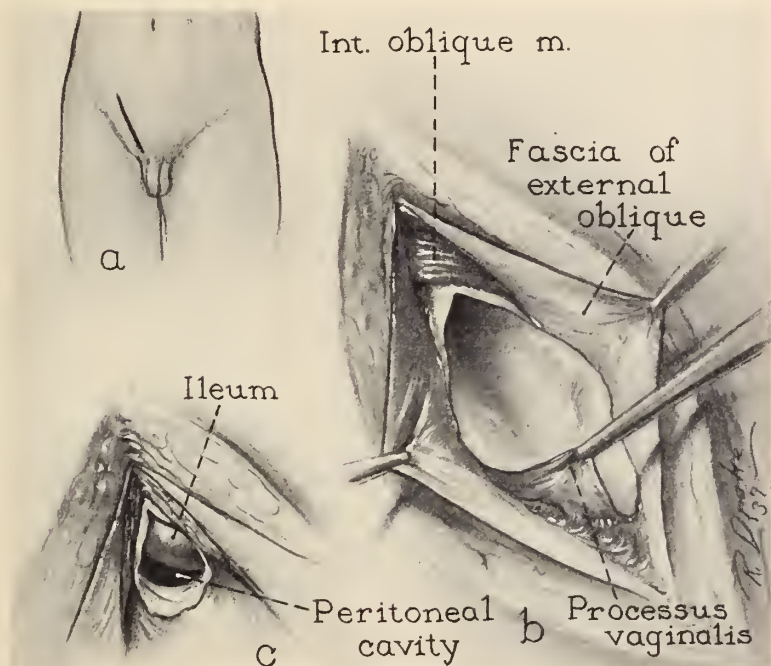
Fig. 1. Multiple stage operation for abdominal cryptorchidism: *a*, The site of incision. *b*, The empty hernial sac open and the point of division of the fibers of the internal oblique muscle indicated by heavy line. *c*, The muscles divided, the incision in hernial sac extended upward, freely opening the perineal cavity, and a coil of ileum shown where it is likely to appear.

3. This will allow the testis to be placed in the scrotum in satisfactory position so that it can be attached to the fascia lata of the thigh, employing the principles laid down by Torek.

It is probably wise to allow the testis to remain attached to the thigh for a period longer than will as a rule be found necessary in the treatment of inguinal and varieties of cryptorchidism other than abdominal. No harm will result if this abnormal, though not inconveniencing, relationship be allowed to remain for a year.

Third stage. The third stage simply consists in the detachment of the

testis from the thigh with the appropriate dressmaking and suture of wounds.

First stage. 1. The inguinal canal is opened by an incision appropriate to the treatment of inguinal hernia. A hernial sac—or unclosed processus vaginalis—may or may not be found. I have seen one patient in whom there was not only an open processus vaginalis, constituting a congenital hernia, but at a slightly lower level, closed off from the processus vaginalis, another sac lined with peritoneum which may be assumed to have been intended to receive the testis though the testis was unable to accept the invitation. If a hernial sac be found, which will occur in something like 80 per cent of the cases, and assuming that no testis is found in this sac up to the level of the internal inguinal ring, the search will generally be aided by the presence, on the posterior wall of this sac, of the vas deferens. In some cases, to this vas deferens will be found attached an epididymis free from any attachment to the testis except at its distal end, where it is united directly to the rete testis. This extremely abnormal relation has, in my experience, been more common in cases of abdominal cryptorchidism than in those of the other varieties. It should, however, be remembered that an abnormal relation between the testis and epididymis, varying from an abnormally long mesorchium up to an almost complete detachment, as above suggested, will regularly be found in cryptorchidism. The vas, with or without the epididymis, having been located, traction upon this structure will lead to the testis if one exists. How frequently complete absence of a testis occurs is not clear from the literature. I have seen it on three occasions, the epididymis ending blindly in tissue which showed no evidence of testicular elements.

2. The testis having been located, the incision should then be enlarged upward, dividing the heavy fascia of the external oblique muscle well above the internal inguinal ring, also dividing the curving fibers of the internal oblique, and freely opening the peritoneal cavity (see fig. 1). This will allow exploration of the abdominal cavity in those cases in which the testis lies so high as to be inaccessible through the inguinal ring and cannot be drawn down to that level by traction upon the vas deferens. In some cases at least, the testis will be found some distance above the internal ring, sometimes attached to the parietal peritoneum and sometimes attached to a coil of intestine, as occurred in one of my cases.

3. The opening in the peritoneum should be sufficiently large to allow the testis to be freed from its attachments under sight and not with the testis under traction. The parietal peritoneum should be divided in such a way as to leave a cuff of peritoneum attached to the testis which will later be used to create a tunica vaginalis. The parietal peritoneum should then be freed from the vas coming from below and the structures of the cord

should be freed from the parietal peritoneum, if necessary nearly to the level of the entrance of these vessels into the renal artery, renal vein, or vena cava, as the case may be. The cord should also be detached from its retroperitoneal attachments, since only in this way can all of the length be obtained which is possible without injury to the vessels (fig. 2). When these steps have been carried out, the testis will, as a rule, lie in the upper portion of the inguinal canal. At this stage the hernial sac, if one exists, should be removed and the sac closed in the usual manner, except that the incision in the peritoneum on the anterior surface will require more extensive suture.
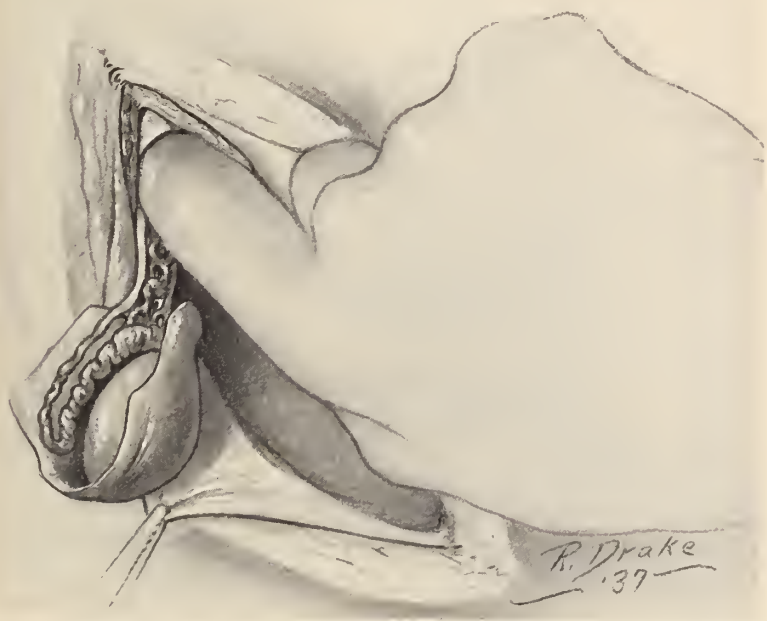
Fig. 2. Showing importance of free mobilization of the spermatic cord from the peritoneum and retroperitoneal tissues by blunt dissection. Note the cuff of peritoneum left attached to the testis for use in reconstructing a tunica vaginalis.

4. The fibrous tissue surrounding the cord in its lower portion, where it has not lain in the retroperitoneal space, should now be removed as thoroughly as is desirable in the ordinary operation for the inguinal variety of this condition. I think it is probably true that, in this group, shortness of the vas deferens will more commonly occur than in the other varieties. If this be true, increased length of the vas should be obtained by double ligation and division of the deep epigastric vessels, with incision of the floor of the inguinal canal so that the vas leads directly upward from its relation to the ureter and seminal vesicles to a point in the region of the external inguinal ring.

5. When these things have been accomplished, the testis should lie comfortably and without undue tension at least as low as the normal position of the external inguinal ring. In some cases, at least, it will lie at a lower level. The tunica vaginalis should be now reconstructed with the intention of producing an hydrocele. (I digress at this point to suggest that, in the operations indicated for other types of cryptorchidism and in which it is proposed to place the testis in the bottom of the scrotum and secure it there, the parietal layer of the tunica vaginalis should be very completely removed in order to avoid the development of hydrocele which, in that condition, would be objectionable while in the abdominal type of retention will assist importantly the second stage of the operation.) The testis should now be anchored to the tissues of the posterior wall of the inguinal canal or to the tissues of the upper portion of the scrotum, posteriorly, just below the level of the spine of the pubis. In thin patients it may be necessary to remove some subcutaneous fat tissue in order to make a bed for the testis and avoid pressure after suture of the overlying tissues (fig. 3).

6. The inguinal canal should now be closed, bringing together all of the layers in front of the testis and the cord.

Second stage. At least one year and perhaps longer should be allowed to elapse between the first and second stage. During this period some degree of hydrocele, occasionally considerable, may be expected to develop. This is desirable.

1. The wound should now be reopened through the scar of the previous operation.

2. The testis should be freed from its abnormal attachments. This will be much facilitated by the development of an hydrocele which will, in the first place, enable the testis to be accurately located without difficulty and, in the second place, much diminish the area over which the testis is attached to surrounding tissues. In my earlier operations I omitted to reconstruct a tunica vaginalis and had to spend an unnecessary amount of time in carefully freeing the testis from its very dense adhesions to surrounding structures since the identification of all of the structures, including the abnormally placed epididymis, is by no means easy.

3. At this point, I am in the habit of dilating the scrotum with the fingers and packing it with gauze, which serves to check any slight oozing which this violent procedure may have caused and also to outline the scrotum so that the appropriate point may be selected for attachment to the thigh.

4. Detachment of the spermatic cord and the vas deferens from their bed, to which they have become adherent, must be carefully carried out. It will generally be necessary to extend the incision as high as at the first stage and, not rarely, a slight pouting of the peritoneum, so as to form the beginnings of a new hernial sac, will be found. The detachment

of the cord from the peritoneum and from the retroperitoneal structures must again be carried out. This having been done, it should as a rule be possible to place the testis in a satisfactory relation to the scrotum without undue tension.

Fig. 3. Showing method of attaching the testis to the posterior wall of the canal, the reconstructed tunica vaginalis and (in insert) the position of the testis at end of first stage of the operation.

5. The principles laid down by Torek are now used in attaching the scrotum to the skin of the thigh and the testis to the fascia lata. The distention of the scrotum with a gauze pack will facilitate the selection of an appropriate point for an incision on its inferior and internal aspect where an oblique incision, as a rule about 3 cm. in length, should be made. This incision should divide not only the tissues of the scrotum, but the

fascial layers of the scrotum itself. The incision in the thigh should be made at a point where the scrotum can be attached without unreasonable tension (fig. 4). The attachment of the posterior lip of the incision in

Fig. 4. Showing relations at the second stage of the operation after the testis and cord have been freed, the posterior lip of the scrotal incision sutured to the superior lip of the incision in the thigh and the testis about to be drawn down for suture to the fascia lata.

the scrotum to the thigh should be accurately made by catgut sutures in such a way that the raw surfaces of each layer are satisfactorily apposed. It is not only proper but desirable to use catgut for this layer since there will be little or no tension on it when the anterior layer is sutured to

the inferior lip of the wound in the thigh.   In the attachment of the testis
to the fascia lata, I object seriously to the technic advised by Torek of
passing the sutures through the tunica albuginea and then through the
fascia lata.   In the first place this can rarely be done without creating
considerable tension.   Either these sutures will rapidly cut through the
tunica albuginea or they will absorb and release the testis.   In the former
event the tubules are exposed.   If even the slightest degree of wound
infection occurs, raveling of the tubules and destruction of the testis will

Fig. 5. Showing placement of sutures in the scar tissue below the testis and
through the fascia lata.

result.   I have seen it occur on various occasions.   The technic suggested
by Wangensteen in which sutures are passed through the tunica albuginea,
but in which a layer of fascia and areola tissue is allowed to remain between
the testis and the fascia lata, seems to me an improvement but not com-
pletely satisfactory.   In a considerable group of cases, most of them
patients with the inguinal variety of cryptorchidism, I have found that a
perfectly satisfactory attachment can be obtained by using some of the
loose tissue about the lower pole of the testis, often lightheartedly referred
to as "the gubernaculum"—microscopic examination fails to show the

presence of muscle fibers in my cases—which will allow satisfactory attachment to the fascia lata of the thigh, leaving a small interval, perhaps 0.5 cm., between the testis and the fascia. Attachment thus made will hold. Retraction of the testis will not occur. Detachment will be made easier. Damage to the testis will be avoided (fig. 5).

Fig. 6. Condition at end of the second stage of the operation

6. The anterior layer of the scrotal wound should then be attached to the lower lip of the incision in the thigh. For this attachment I have used a variety of suture materials, beginning with catgut, which is worthless, and then using silk, which did not seem to me satisfactory in that mild degrees of irritation often occurred and the sutures cut through under the influence of rather mild tension. I have now for some time used either silkworm gut or dermal according to the age and size of the

patient. At the completion of this stage, a small piece of gauze should be drawn through between the scrotum and the skin of the thigh to prevent the apposition of skin surfaces (fig. 6).

Third stage. It is satisfactory to undertake the detachment of the testis from the thigh after three or four months in most cases of inguinal cryptorchidism. In the case of the abdominal cryptorchid, it has seemed to me wiser to leave it attached for at least six months, perhaps even a year, where the operation has been done in stages and the testis has occupied a high position.

1. The skin of the scrotum should be freed from the thigh and, if the attachment of the testis has been done as above suggested, no danger will arise of injuring the testis or any of its accessory structures. If sutures have been inserted into the tunica albuginea, this part of the dissection must be carried out with great care to avoid injury to the tunica albuginea.

2. Detachment having been made, the skin of the scrotum should be trimmed to a semicircular wound so as to avoid the development of dogs' ears which are unnecessary and unsightly. The skin of the scrotum can very conveniently be closed with a subcuticular suture which gives excellent apposition and overcomes the universal tendency of the dartos to roll in the skin edges where interrupted or continuous over and over suture is used.

3. The wound in the thigh is closed with interrupted sutures.

ILLUSTRATIVE CASES

There follow brief accounts of four patients upon whom this operation has been carried out in whole or in part:

Case 1. A boy of eight first registered at the clinic on June 25, 1934. He was a full-term child, birth weight being $7\frac{1}{4}$ pounds (3.3 kg.). It is known that neither testis has been visible since birth. Otherwise his history has been negative.

Examination. Height 4 feet $1\frac{1}{2}$ inches (127 cm.); weight 57 pounds (26 kg.). Well developed and nourished. Tonsils missing. Teeth, many filled cavities. Slight cervical glandular enlargement. Examination negative except that neither testis is palpable.

Surgical consultant. "I cannot feel the testis on either side. The scrotum is rather more developed than I should expect. Operation advised."

Operation. June 27, 1934. Preoperative diagnosis: bilateral cryptorchidism, probably abdominal. Incision on the right side showed the inguinal canal normal except that there was no sign of spermatic cord, vas, or testis. A small sac was found at the level of the internal ring. Upon extending the incision upward, testis found lying free in the abdominal cavity about 5 cm. above the internal ring. It could be brought down just through the ring. After freeing it from the peritoneum and freeing

the vessels from their retroperitoneal attachment, it was possible to bring the testis down to about the level of the external ring. Some additional length for the vas was obtained by dividing the tissues on the posterior wall of the canal down to the level of the deep epigastric artery. As it did not seem wise to put any more tension upon the vessels, the testis was attached to the posterior layer of the inguinal canal at about the level of the external ring. At this time it seemed as though the vas was seriously short. An almost exactly similar condition was found upon the left side and treated in a similar fashion. Convalescence uneventful.

Fig. 7. The position of the right testis is not clearly shown as it is obscured by the pulling of the scrotum to the left. On the left side the testis just at the attachment of scrotum to thigh.

Readmission. Returned for further operation June 19, 1935. Both testes can be felt at about the level of the external ring. They seem of normal size.

Operation. Second stage: Incision through the scar of previous operation on the right. Testis found imbedded in scar tissue and freed with considerable difficulty. When this was accomplished, however, the freeing of the cord was relatively simple and sufficient length was readily obtained to place the testis in the bottom of the scrotum. In freeing the upper portion of the cord, a slight redevelopment of the hernial sac was found and dealt with. The testis was then attached to the fascia lata of the right thigh, using the principle of Torek. Similar operation on the left side, but here the testis was considerably larger than at the

previous operation. No difficulty experienced in getting sufficient length to carry out a satisfactory Torek type of operation.

Postoperative Course. After such operations, it is, of course, necessary to keep the knees held closely together during the first week or ten days of convalescence. On this occasion, the towel fastening the knees together became loose during the first night of operation and detachment of the right side occurred. In other respects the convalescence was uneventful. At the time of dismissal, July 3, it was noted that on the right side the testis was in reasonably satisfactory position but somewhat higher than desirable owing to the detachment from the thigh. On the left side the attachment was satisfactorily healed.

Readmission. Returned for final operation on October 31, 1935. Right testis then in excellent and normal position. Left still attached to the thigh and in good position (fig. 7). Two days later it was detached and it was noted that the size of both testes seemed to be normal.

Has not since been seen at the clinic, but in October, 1937, his father reported to me that he appeared normal in all respects with testes in normal position and scrotum well developed.

Case 2. A boy of sixteen registered August 31, 1935. Operation for appendicitis in 1930. Always supposed to be well and normal until an attack of mumps in the spring of 1935. At this time it was noted that neither testis was in the scrotum, though the boy's development was in other respects normal.

Examination. Well developed and nourished. Examination entirely negative except for the scrotum which was small and underdeveloped. Neither testis could be palpated. Preoperative diagnosis of bilateral cryptorchidism, probably abdominal. Operation advised.

Operation. September 2, 1935. Incision over the right inguinal canal showed abnormality of the external ring which appeared to be missing. Incision through the fascia of the external oblique showed the canal occupied by what appeared to be a hyperplastic epididymis. The upper portion of the canal showed a congenital hernial sac occupied by this epididymis. Incision extended upward dividing the external and internal oblique and opening the abdomen. Testis was found adherent to a coil of ileum and to the parietal peritoneum at a point about $3\frac{1}{2}$ inches (9 cm.) above the internal inguinal ring. The testis seemed definitely larger than was to be expected at the patient's age; vessels very short, as would have been expected. After extensive freeing of the vessels from their retroperitoneal attachment, the testis could be made to lie comfortably at the level of the external ring, at which point it was attached to the posterior tissues. Hernia repaired and wound closed, bringing all the tissues together in front of the cord. An almost exactly similar situation found on the left except that the testis was smaller and

attached to the parietal peritoneum at a somewhat lower level, about 5 cm. above the internal ring. It was freed with somewhat less difficulty, but could not be brought into the scrotum. Convalescence uneventful.

Readmission. Returned for further operation June 8, 1936. Nothing important in history during interval. Examination negative. Both testes could readily be felt lying at the level of the external inguinal ring.

Operation. June 8, 1936. Incision through the scar of the previous operation on the right. Testis found very adherent to all surrounding structures and considerable time was consumed in freeing it. Testis was of good size and consistency. After freeing the testis, no great diffi-

FIG. 8. Showing the very satisfactory position of the right testis in September, 1936. The left testis was brought down just after this picture was made.

culty was experienced in freeing the vas and the vessels so that sufficient length was obtained to place the testis in the bottom of the scrotum. It was attached to the fascia of the right thigh by the principle of Torek, the sutures attaching the testis to the fascia lata being passed through fibrous tissue below the lower pole of the testis. This operation was so time-consuming that it was not thought wise to operate upon the left side at this time.

Operation. Returned for further operation September 28, 1936. Right testis found in excellent position. It was detached from the thigh and the wound sutured (fig. 8). Operation similar to that done upon the right

side carried out upon the left. Convalescence uneventful. It was not thought necessary for the patient to return here for detachment of the left testis, which was carried out by his surgeon at home.

Postoperative Course. Report from the boy himself in August, 1937, showed condition apparently entirely satisfactory with scrotum normal and testes well at the bottom.

Case 3. A boy of fifteen first registered June 19, 1936. Third child, birth normal. First teeth normal. Second teeth slow in coming. At about the age of seven, parents first noted that the child was smaller than the average. Started school at five and one-half years and had an average record. At the age of fourteen, it was first noted that neither testis could be found in the scrotum. In February, 1936, was treated with antuitrin S, about 40 injections with a total of 1500 units. Apparently as the result of this treatment, a swelling appeared in the left groin accompanied by some discomfort. History otherwise negative except for headaches relieved by glasses.

Examination. Height 4 feet $8\frac{1}{2}$ inches, or 144 cm. (average boy of fifteen years, 5 feet 4 inches). Weight 67 pounds, or 30.4 kg. (average 120 pounds). Appeared like a boy of about ten years. Symmetrically built and fairly well nourished for that age. Voice high pitched. Secondary sex characteristics undeveloped and no testis could be felt in the right inguinal canal. On the left side, what was thought to be a testis could be felt in the mid-canal. Operation advised.

Operation. June 29, 1936. Preoperative diagnosis: bilateral cryptorchidism, right abdominal, left inguinal (?). Incision over right inguinal canal disclosed a congenital hernia, with well-developed processus vaginalis but no testis. There was apparent closure between an empty tunica vaginalis and the processus vaginalis. Incision extended upward and vas deferens found in the upper portion of the hernial sac. Peritoneal cavity freely opened and testis found lying about 8 cm. above the internal ring adherent to the anterior parietal peritoneum. Testis freed from the peritoneum and vessels freed from their retroperitoneal attachments. They were very short while the vas was of very ample length. Length of the vessels permitted the testis to be brought to the level of the external ring but not safely to a lower point. It was attached to the posterior tissues at that level, a bed having been made for it in the fat tissue so as to avoid pressure from the fascia of the external oblique. Incision on the left side showed that what was believed to be the testis lying in the inguinal canal was an apparently very hyperplastic epididymis. Following this upward through the hernial sac, the testis was found in an almost exactly similar position to that upon the right. Both testes were much larger than normal for the boy's age, and this, taken in connection with the very abnormal epididymis on the left, suggests an effect from treat-

ment with antuitrin S. On this side, operation was similar to that upon the right except that, owing to the difficulty previously experienced in these operations of freeing the testis at the second operation, it was thought desirable to leave enough of the parietal peritoneum attached to the testis to enable a tunica vaginalis to be reconstructed. The testis was attached at about the level of the external ring and the parietal peritoneum, which had been left attached to the testis, was used to reconstruct a tunica vaginalis.

Readmission. Returned for further operation June 1, 1937. During this period the boy has gained 16 pounds (7.3 kg.) and grown 4 inches (10 cm.). His mother feels quite clear that his voice is importantly lower. This opinion is confirmed by the medical consultant who saw him on the previous occasion. He is still a small underdeveloped boy for his age, which is now sixteen.

Operation. June 1, 1937. Operation done upon the right side through the scar of the previous operation. The accumulated scar tissue was excessive, and considerable difficulty was experienced in freeing the vessels and getting full length. It appeared at the time that the circulation had perhaps been somewhat compromised, but a Torek type of operation was carried out. It did not seem wise to operate upon the left side at the same sitting.

Operation. Further operation on June 25, 1937. This was done upon the left side, and incision through the scar of the previous operation showed a considerable hydrocele which had resulted, as intended, from the previous operation. This made the freeing of the testis importantly easier and, on this side, full length was obtained without difficulty. A Torek type of operation was carried out.

Postoperative Course. The patient was dismissed from the clinic on July 10, 1937. At this time it was noted that the right testis seemed somewhat smaller than at the time of operation, to this extent confirming the view that the circulation had been somewhat compromised. On the left side the testis was of good size and in good position. It was advised that operation for freeing the testes should be postponed for about a year.

Case 4. A boy, fourteen years, first registered at the clinic September 17, 1931. History quite normal. Full-term child, instrumental delivery, birth weight $7\frac{3}{4}$ pounds (3.5 kg.). Testes never descended. In recent months, some pain in right inguinal region. Unaware of any hernia. In 1930, physician said heart was irregular but more recently reported it normal.

Examination. Height 4 feet $6\frac{1}{4}$ inches (138 cm.). Weight 67 pounds (30.4 kg.). Well developed and fairly well nourished. Several teeth carious. Heart, slight apical heave, rough blowing systolic murmur over

entire precordia, best heard along left sternal border and just below pulmonic area, poorly transmitted to axilla. Murmur also noted in intrascapular region posteriorly. Pulmonic second sound accentuated. No clubbing of fingers. Right testis low in inguinal canal, associated with inguinal hernia. Left testis not palpable. Operation for hernia and replacement of the right testis and exploration of the left inguinal region advised.

Operation. September 21, 1931. Preoperative diagnosis: bilateral cryptorchidism, right congenital inguinal hernia. Incision over the right inguinal canal. Testis found in sac of congenital hernia lying at level of external ring. It was readily freed from the hernial sac and fibrous tissue about the cord removed so the testis would lie readily in the bottom of the scrotum. Inguinal hernia repaired. Testis held in the bottom of the scrotum by a catgut suture passed through the tissues of the gubernaculum, brought out through the bottom of the scrotum and attached to a perineal crutch so as to maintain constant traction. On the left side, incision over the inguinal canal showed the canal normal except for a small hernial sac which contained a portion of the vas at its upper end. Traction on the vas drew a normally developed testis from the abdominal cavity. After freeing the vessels to the greatest possible extent, particularly from their retroperitoneal attachments, it was not found possible to bring the testis below the level of the external ring. It was, therefore, attached at this level and the hernia repaired and the wound closed.

Readmission. Patient returned on August 20, 1934, after receipt of a letter urging further examination. He remained small for his age and now weighed only 86 pounds (39.0 kg.). Heart found slightly enlarged, with a rough systolic murmur over the apex. Right testis in normal position. Left testis readily palpable in region of external ring, where it was left at the previous operation. Patient declined further operation at that time and has not since been heard from.

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THE TREATMENT OF KIDNEY INFECTIONS IN INFANTS AND CHILDREN

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I cherish very much the privilege of contributing to this volume honoring my dear friend, Dr. Edwin Beer, who is unquestionably one of the world's most illustrious urological surgeons.

Nature has endowed the urinary tract with a fortunate accessibility to scientific investigation and man has created instruments and methods of precision through which the anatomical configuration, as well as the physiological processes and pathological derangements, can be accurately determined. The past fifteen years have witnessed a direct application of technical refinements to the study of the urinary tract in infants and children and this conquest has been one of the outstanding achievements of modern medicine. Accuracy has supplanted speculation. Whenever some urinary dysfunction occurs, prompt investigation, as is customary in the adult, is now prescribed with equal simplicity and effectiveness, far less troublesome reactions, and without danger.

The child is subject to practically the same urinary diseases as the adult and should receive similar investigation. This should not be delayed since procrastination is responsible for the development of destructive lesions and these should be prevented. Urinary disorders contribute tremendously to diseases of infants and children and are responsible for many invalids and a very high mortality rate. Prompt study and corrective therapy would exert a decided influence in reducing the infant death rate.

By far the most frequent condition affecting the urinary organs is infection. There have been about fifteen hundred cases of renal infection in the St. Louis Children's Hospital, or one in every fifty cases; that is, of every fifty patients who entered the hospital one had either an infection on admission or developed it during the stay. This incidence alone pronounces its importance.

The majority of such infections are acute, the so-called acute pyelitis, not really a pyelitis, but a definite pyelonephritis. Since most of these infections are blood borne it would be hard to conceive of a simple involvement of the pelvis alone; the pelvis, however, plays an important part in the creation and perpetuation of the disease, since it is through the blockage of its outlet by edema and inflammatory reaction that proper

drainage is interfered with. Septic material is thereby retained in the pelvis and pressed back through the secreting surface of the kidney. Many observers fail to give this its true significance. The majority of these acute lesions are associated with preexisting infections such as otitis media, upper respiratory disorders, pneumonia, tonsillitis, and intestinal complaints. It is striking that in the Children's Hospital of the thirty-seven cases of vaginitis only one was complicated by renal infection which bears definite testimony to the hematogenous origin of such renal infections.

Pyelitis in early childhood is very serious. In 88 per cent of the patients examined it occurred in the first decade of life and of nine hundred and nine cases examined several years ago one hundred and seventy-two presented such infections in the first year of life and 40 per cent of these died, death being induced in many instances by other constitutional disorders, but the kidney was often responsible.

I shall not detail the symptoms of acute pyelitis but will simply accentuate a few important features. The onset is usually sudden, characterized by high fever, seldom chills as in the adult; the kidney or possibly both organs may be swollen, but the tenderness so common in the adult is not witnessed, as a rule, in the child. Vomiting and abdominal distention (the G. I. type) are exceedingly common and often are so pronounced as to give the impression of some primary abdominal condition. Occasionally the symptoms are of the cerebral type, that is, pronounced toxemia with stupor, sometimes with convulsions. The leucocyte count is strikingly high, running frequently between twenty and twenty-five thousand, much higher than in the adult. The most characteristic and important finding is to be gained by a urinalysis; pus is almost invariably present and, as a rule, a bacillary type of organism, usually of the colon bacillus group, is present. The urine during the very acute stage may not be particularly purulent, exhibiting only a haze, but the microscope will tell the story. If this is the child's first attack an obstructive lesion may not have been preexisting. If recurrent, one has to be particularly careful in the interpretation of the picture, since what might appear to be an acute unilateral kidney condition alone may be the result of an obstructive lesion in the lower urinary system with both kidneys involved in the infectious process and only one manifesting the acuteness.

The treatment of acute pyelitis consists, as a rule, in the free administration of fluids by needle and mouth, careful attention to bowel action, the correction of toxemia and acidosis, and the administration of urinary antiseptics. Such therapy usually requires from one to three weeks to produce relief, in the course of which time the infection which has been pent up in the kidney, due to inefficient drainage of its pelvic outlet, may be cleared. I feel confident, however, that it would be much more judicious, particularly in the very acute cases, to evacuate the pelvic contents with

the ureter catheter, a procedure which is simple and without danger. The acuteness usually subsides in a few days and sometimes within twenty-four hours. It seems certain that the retention of septic products in the kidney tissues is bound to exert a bad influence and create scars and disturbances which will be responsible for later reactions, particularly stone and obstructions. Since infections occur in girls three times as frequently as in boys and since the pyelitis of pregnancy is a very frequent cause of infections in the kidney in later life, we may naturally infer that these preexisting lesions prepare the soil for the lowered resistance of obstruction later.

The recent use of sulfanilamid has been productive of very striking results. I have been informed by Dr. Hartman of the Children's Hospital that recovery is much more rapid, requiring several days to a week instead of several weeks, as has been customary under other urinary antiseptics. The drug requires very careful administration and demands vigilant observation of the patient during its administration. In the hospital the dosage has been exceedingly high in proportion to what is usually given in current practice. It has been my experience in the usage of the drug that smaller doses have been as effective as massive ones. The new soluble preparation of sulfanilamid with citrolactate seems to prevent the toxic disturbances which have been so frequently observed during the administration of sulfanilamid, even if alkalies were simultaneously given. This soluble mixture has seldom been attended by toxic symptoms even in children and adults who could not tolerate the drug before. At any rate, this drug carefully administered offers a brighter prognosis to the acute renal infections. But I still believe that prompt evacuation of the pelvic contents with the ureter catheter in association with such a drug would be the superior method of treatment.

A physician in Illinois, who has medical charge of a reformatory for boys, told me that pyuria and albuminuria were frequent findings and that almost invariably there had been a previous history of pyelitis. Dr. Hartman found in his follow-up analysis of patients who had previously been subjects of pyelitis that practically all were free from infection unless there was interference with normal drainage.

CHRONIC INFECTIONS

Chronic renal infections create the most frequent demand for urological investigation and therapy. The sole function of the excretory ducts of the urinary tract is to deliver accumulated urine without impediment. Unfortunately obstructive conditions along the urinary pathways occur with considerable frequency and are responsible for stasis on a great many occasions. The most frequent sites of obstruction are at the ureteropelvic juncture, the intravesical ureter and the internal orifice of the bladder, the latter the most frequent.

Therefore, the treatment of chronic kidney infections in children involves the following:

1. The determination of the presence of an obstruction and its location.
2. Institution of drainage.
3. Topical applications.
4. The administration of internal medication.
5. Supportive measures.

Children harboring chronic urinary infections have never, as a rule, been in good health; they are poorly developed, or are subjects of intermittent recurrent attacks of urinary infections with febrile reactions. They frequently are presented to us in various stages of uremia and sepsis after having been administered to, often since early childhood and even by competent pediatricians.

Persistent pyuria or the continuance of symptoms representing urinary infection should immediately command a prompt investigation. Even if the infection has a tendency to abate, particularly with the employment of some of the newer drugs, like sulfanilamid, injustice is being done to the child because the mechanical lesion creating distention of the upper urinary system even without infection is progressive and the later recurrence of infection will find the kidney much more damaged.

The following figures represent the various obstructive lesions which are responsible for the persistence of infection.

Figure 1 is a representation of a type of obstruction occurring at the ureteropelvic juncture. Such obstructions are less frequent than at other locations but are more serious. The majority of these patients appear with marked hydronephrosis or pyonephrosis, and many require nephrectomy. Children are extremely ill and septic with such pyonephrotic lesions. In such cases nephrectomy, if necessary, is preferably performed by a two-stage operation. Simply drain the kidney at the first operation, allow the child to recover and remove the organ secondarily in a short time. This procedure is a life-saving one, since primary nephrectomy under such conditions is extremely hazardous.

Obstructions at the ureteropelvic juncture are not susceptible to dilatation with the ureter catheter or bougie. They are usually the result of congenital stricture, valves or aberrant vessels, and manipulative measures are ineffective. Occasionally, if the kidney is not too badly destroyed, plastic procedure between the pelvis and upper ureter can be utilized, as in Figure 1, which represents a large hydronephrosis, stricture at the ureteropelvic juncture, resection of the ureter, resection of the pelvis and anastomosis of the ureter to the dependent part of the new pelves. The important surgical points in this operation are: accurate approximation of the two surfaces, careful splinting over a soft rubber catheter with very little suturing at the line of union, and free drainage through the kidney above.

Owing to the tendency of this type of case to be bilateral, one should make every effort to spare the kidney by such plastic procedures whenever it is possible.
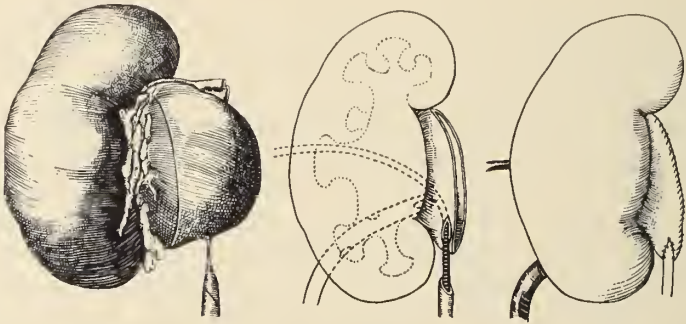
FIG. 1 (see text)
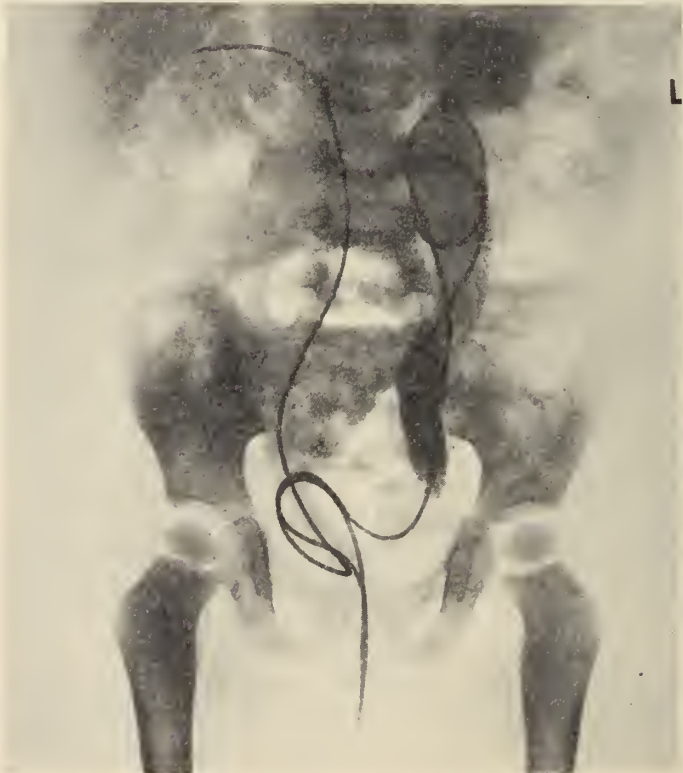
FIG. 2. Obstruction of the left intramural ureter

Figures 2 and 3 (A & B) represent obstruction at the lower end of the ureter, Figure 2 being an obstruction in the intramural ureter on the left

side with considerable hydroureter and hydronephrosis with infection, which was promptly relieved by ureteral dilatation and drainage. Such obstructions usually occur within the bladder wall, occasionally without, and result from congenital sclerosis. Infections resulting from such obstructions located in this neighborhood do not produce early destructive kidney lesions and are often times correctible by dilatations with ureter catheters and bougies, drainage and topical applications. The ureter takes up the slack and spares the kidney pelvis. Dilatations must be repeated and persistent. The indwelling catheter for drainage and topical applications is occasionally advisable and is very beneficial. Whenever the obstruction is pronounced and resists dilatation the relief must be accomplished by open surgery. Since the majority of these obstructions are intramural, I have found the transposition operation, which I described in 1919, to be very effective. This operation is entirely intravesical; it simply means the excision of the intramural ureter leaving its normal attachments to the bladder wall as it enters. This is certainly superior to ureterovesical anastomosis which must never be done through choice, since it is almost inevitably productive of renal death through stricture.

The most frequent cause of chronic pyelitis in infants and children is obstruction at the internal orifice of the bladder either through valves or contractures, occurring about equally in boys and girls. I have seen about thirty-five such cases representing this lesion. Most of these children have been chronic invalids since infancy and have carried a continuous or intermittent pyuria. Over one-half were under 5 years of age. The great majority presented definite symptoms of urinary disorder— frequency in over 50 per cent, pain and burning on urination in about 25 per cent, gross pyuria in over 70 per cent, uremia in 30 per cent. Residual urine was present in over 80 per cent of all the patients. Fifty per cent had over 100 c.c., 12 per cent over 500 c.c. In but few instances had residual urine or bladder neck obstruction been suspected. Owing to the frequency of bladder neck obstruction in infants and children as a cause of chronic pyelitis, it should always be suspected and can be so easily determined by the practitioner of medicine. The simple passage of a catheter after voiding will, without any danger to the child, if properly performed, give a clue to the situation. The presence of residual urine with infection interferes with the normal coaptation of the ureterovesical valve which protects the ureteral orifice from regurgitation. This valve becomes stiffened and stretched, loses its competency and the ureter and renal pelvis become a common cavity with the bladder. As the backpressure increases, the ureter and pelves are distended and the renal substance encroached upon. As this progresses, uremia becomes imminent. On many occasions one kidney will present a clinical picture of an acute infection and in some instances I have known its removal when it only represented one part of the picture, the other kidney being equally dis-

turbed and often more pronouncedly involved. Hence the necessity for careful investigation.

In all of these chronic infections, particularly with residual urine nitrogen, retention should be determined. If it is elevated, we must assume that both kidneys are involved. The cystogram affords the most valuable information in that it will show regurgitation up one or both ureters, and whenever regurgitation occurs with filling of the bladder, a bladder neck obstruction is almost invariably present. Treating the kidneys through catheter drainage or surgery is missing the point. Intravenous urography may be helpful but it is not nearly as valuable as cystographic study. The cystoscope gives the final diagnosis as to the nature of the lesion and of associated phenomena and should always be

A   B

Fig. 3 (see text)

used in such cases. It is absolutely without danger. In several hundred cases, in which I have used it in such children, I have yet to see a single case materially disturbed. As a matter of fact, the reactions in children are exceedingly rare. Post cystoscopic complications are negligible. Only 35 per cent require anesthesia and, if an anesthetic is given, it is simply administered for a few minutes during the early part of the manipulation. I, therefore, cannot urge too strongly a prompt investigation of the urinary system in infants and children.

Figures 3A and 3B show a pronounced pyelonephritis with regurgitation up the right ureter, but not the left. Contracture of the vesical neck had broken down the right ureterovesical valve but the left orifice was occluded by a congenital stricture, as is seen in the illustration. In other words,

there was a double mechanical cause for the persistence of pyelitis which required not only the relief of the vesical neck obstruction by means of the baby punch, but dilatation of the left ureteral obstruction as well, and drainage and topical applications to the kidney.

Figure 4 represents the case of an infant extremely sick, with clinical evidence of a right-sided pyelitis. Investigation, however, showed that

FIG. 4 (see text)

there was a contracture of the vesical neck, regurgitation up both ureters and bilateral distention with infection. Correction of the neck obstruction with the baby punch and relief of bladder stasis cured the renal infection.

Figure 5 shows regurgitation up the right ureter. This patient had been thoroughly investigated by a competent urologist who found a double ureter on the right side with infection, hydroureter and hydronephrosis

of the upper kidney pelvis and its ureter. Heminephrectomy was advised. When I saw this child I found that there was a vesical neck obstruction, the result of a valve. There were three ounces of residual urine and an open regurgitant orifice of this infected ureter and pelves. Resection of the valve at the bladder neck by means of the baby punch promptly cured the renal infection and the kidney did not require surgery.

Fig. 5 (see text)

Figures 6A and 6B represent a chronic pyelitis of six years' duration since infancy. There were contracture of the vesical neck, regurgitation up both ureters, and marked dilatation of ureter and kidney pelves. There were six ounces residual urine. The patient was cured by removal of the contracture at the internal orifice of the bladder. A cystogram seven years later shows a normal bladder with no regurgitation up the ureters, illustrating Nature's remarkable power of recovery of even such

delicate structures as ureterovesical valves when infection and back-pressure are relieved.

Figures 7 and 8 represent extreme dilatation of the ureters and pelves. Both children were uremic and septic. Both were suffering with incontinence of urine, one having 250 c.c. of residual, the other 1000 c.c. Both cases were the result of contracture of the vesical neck with broken incompetent ureteral valves. After preliminary catheter drainage for relief of uremia and sepsis, I removed the obstruction, a contracture of the neck in both instances, by means of the cautery punch, and both were promptly relieved of their urinary infection. The last case exhibits the

A   B

FIG. 6 (see text)

most pronounced dilatation and tortuosity of the ureter, practically filling the abdomen. The child was bedridden, profoundly uremic. It required several months of preliminary drainage with the catheter. And, by the way, these bladders in children carrying high residuals must be drained in a manner exactly similar to the prostatic and relieved of their sepsis and uremia before any investigation or operation is undertaken. This child had never passed but one-half ounce of urine at a time in his life and had dribbled almost constantly for a year. After the simple removal of three small pieces of contracture of the vesical neck with the baby punch, this boy within twenty-four hours, voided nine ounces,

his first voiding after the catheter was removed. It is now three years since the operation. He is in perfect health. In fact, within three weeks after the operation his urine had cleared completely, which is almost unbelievable in the face of his long-continued infection. It has remained

FIG. 7 (see text)

clear. This is the condition of tremendous ureters with angulation and infection which some men attribute to neurogenic disturbances, others to primary infection of the ureter, but which are so much more easily explained by obstruction at the bladder neck with regurgitation. The proof is that they are cured by the relief of the obstruction.

Some surgeons have gone so far as to advocate tremendous abdominal operations to straighten out the kinks of the ureter, remove sections, and to reanastomose the canal. Such surgery has no foundation. It is treating the effect and not the cause; it is offering no chance of cure and

Fig. 8 (see text)

is attended by a tremendous mortality, whereas the relief of obstruction at the neck, which is the cause of this condition, is very simple and is accompanied by no mortality whatever.

I urge the reader to seek a prompt investigation as to the cause of chronic pyelitis, in infants and children, which has resisted the usual

medical therapy. Some mechanical obstruction producing stasis is usually responsible. This must be corrected early to protect against destructive lesions of the kidney which may progress beyond the possibility of a cure.

Early diagnosis and corrective therapy will serve to protect many children from chronic invalidism and to lessen the infant death rate materially.

Other less common urinary infections, such as those occurring with stone, tuberculosis, tumors, etc. will not be considered in this discussion.

CANCER OF THE UROGENITAL TRACT[1]

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Before discussing the particular problems relating to cancer of the urogenital tract, I should like to discuss the general problem of cancer as given in the following outline:

General Consideration of the Problem of Cancer in Urology

A. The varying degrees of malignancy:
    I. Potential lesions.
    II. Precancerous lesions.
    III. Malignant lesions.
        1. The grades of malignancy
            Broders' classification
            Life history (duration from onset to death).
        2. Metastases
            By invasion
            By lymphatics
            By blood stream.
B. The varying application of treatment:
    I. Only two methods are recognized as effective:
        1. Irradiation.
        2. Surgery.
    II. These are variously applied:
        1. Palliatively (to relieve symptoms)
        2. Conservatively (to prolong life)
        3. Radically (to cure).
C. Relation of A to B:
    I. The degree of malignancy in relation to irradiation.
    II. Radical surgery in relation to metastases.
    III. The value of statistics on the basis of a five-year cure.
    IV. The significance of an early diagnosis.

The variability in the degree of malignancy is recognized by the terms precancerous lesions, potential cancer, and malignancy. Malignancy of the urogenital tract in itself shows variability in degree. By variability is meant the differing periods required for the particular type of cancer to kill the patient, if untreated, and the classification of the tumor as to its degree of malignancy, according to the extent of full differentiation of the different cells comprising it, is of value. Broders has suggested four grades: in Grade One, 75 per cent or more of the cells are fully differentiated into adult forms; Grade 2, between 75 per cent and 50 per cent; Grade 3,

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between 50 per cent and 25 per cent, and Grade 4, less than 25 per cent; in other words, in Grade 4 over 75 per cent of the cancer cells show active mitosis.   Classified in this way, and knowing the type and location of the cancer, one can infer the life history of that particular cancer, and predict the average period of time required for it to kill the patient, if untreated. It seems to me that this is a very important consideration in the problem of treatment.   It helps to select the type of treatment best suited to the individual.

The second consideration of recognized importance in the selection of treatment is the presence or absence of metastasis.   Cancer spreads by direct invasion, by the lymphatic system and by the blood stream.   The first fact that one wants to know after the diagnosis of cancer has been made is whether any of these types of metastases have occurred.

The third consideration is the choice of that one of the various methods of treatment for cancer which will give the best result in that particular case.   At the present time only two methods at all successful in the treatment of cancer are recognized.   One is irradiation, either by radium or X-ray, and the other is radical surgery, by which is meant the total removal of the cancer before it has spread beyond its local point of origin.   Surgically, if cancer is removed before metastasis occurs, a cure is effected. Irradiation and surgery have been applied so variously in the treatment of cancer of the urogenital tract that much dissension has arisen with respect to the choice between them for the initial treatment.   This confusion has been added to by the advent, more or less recently, of a new surgical procedure, namely transurethral resection, particularly when applied to cancer of the bladder and prostate.

The variable application of the two recognized methods of treatment may be grouped under the headings palliative treatment, conservative treatment, and radical treatment.   By palliative treatment is meant an attempt to relieve symptoms without any effort to cure the patient.   The fact is recognized that this cancer is incurable.   Conservative treatment, on the other hand, has in mind an attempt to prolong life beyond the period in which the cancer, if untreated, would kill the patient.   Radical treatment is an effort to cure the patient of cancer, so that when he dies cancer will not have been a factor in any way in his death.   These three considerations should be taken seriously in outlining any treatment for any type of cancer.   The decision should be made at the outset whether treatment is to be palliative, conservative, or radical.

With these things in mind, one can more clearly correlate the various degrees of malignancy and their subsidiary considerations with the various types of treatment and their subsidiary considerations.

First is the theoretical correlation of the degree of malignancy with the probable response to irradiation.   It is a fact that, in some cases, the more malignant the tumor, the more radiosensitive it is, and, as a rule, the less

malignant tumors are more radioresistant. In considering irradiation one should distinguish between the reaction of the tumor, as shown by its apparent clinical disappearance, and its absolute destruction, that is, between radiosensitivity and radiocurability. Some tumors are definitely radiosensitive but are never cured, whereas others are radiosensitive and likewise radiocurable. Growing experience in irradiation enables one to classify a considerable number of tumors according to their degree of malignancy, their life history and their reaction to irradiation, whether radiocurable, radiosensitive, or radioresistant.

All of these points help in the selection of the type of treatment. In general, however, they are disregarded. With the advent of irradiation there has been a general tendency to delay radical surgery until after metastases have occurred and it is too late to cure the patient by surgery. If radical surgery is to be used, it should be used early. Suspicion of cancer should be aroused in an early stage and this suspicion should be confirmed promptly by microscopic study so that the tumor can be classified as to its life history and probable response to irradiation. If its life history is short and it presumably will not respond to irradiation, then is the time for radical surgery, and it should not be put off until later when cure of the patient by any method is impossible.

Another consideration in respect to the cure of a patient with cancer is the relation between the period of time used as a criterion of cure and the life history of the cancer. Some cancers, even though untreated, have a life history of anywhere between five and ten years. Most cancers, however, will kill the patient in a much shorter time. This should be recognized so that we may have some idea of the value of the statistics of five-year cures. Most statistics with respect to a cure of cancer of the prostate are based on a five-year cure, but there are many cancers of the prostate that have a life history of over five years. There are, to be sure, a great many cancers of the prostate that will kill the patient in less than five years, but an arbitrary period of five years requires reservations. In some types of cancer, statistics of five-year cures are of less value than in other types.

One should keep in mind the importance of an early diagnosis in cancer. By early diagnosis we mean one made when the cancer is localized, before metastases have occurred and, of course, before irradiation. With the advent of irradiation the effort to make early diagnoses seems to have weakened considerably. Previously the whole surgical profession was more or less active in the education of the public in the advantages and necessity of an early diagnosis. What woman nowadays hesitates to seek counsel the moment she feels a lump in her breast? The public knows that the earlier the diagnosis the more certain is a cure. I am sure that if we could get every person who has a lump in his testis within a month after onset of that lump, we could cure about ninety per cent of testicular tumors

by simple orchidectomy.   The average time when the patient is first seen
is over five months and by then metastases have occurred in many.   The
first object in radical treatment therefore is early diagnosis.   A great many
men nowadays unfortunately do not believe in surgery for cancer.   If
irradiation does not relieve the patient, and complications occur, or symp-
toms arise, only then is an attempt made to relieve the complication or
symptoms.   This means that a great many men who treat cancer are
treating it palliatively or conservatively and are not attempting to cure
the patient.   These men belittle the value of an early diagnosis and some
even go so far as to speak of the effort to make early diagnoses as deceptive
propaganda.   I firmly believe that we should keep our propaganda active
with respect to the early diagnosis of cancer.   Let us now discuss these
points in relation to the special forms of cancer of the different parts of
the urogenital tract.

Tumors of the kidney are divided into tumors of the renal parenchyma
and tumors of the pelvis and ureter.   The classification of parenchymal
tumors today is not at all uniform.   There is considerable difference of
opinion amongst pathologists as to the proper classification of many of
these tumors.   The following outline is more or less of a makeshift and is
as simple as possible.

<div align="center">

Tumors of the Renal Parenchyma

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Classification	Incidence	Average Life
1. Epithelial:		
a. Adenoma..	3%	
b. Carcinoma...	80%	2–3 years
2. Connective tissue:		
a. Benign...	Rare	
b. Malignant (mixed tumors)......................	12%	
3. Embryonal:		
a. Benign...	Rare	
b. Malignant (Wilms's).............................	4%	
4. Hypernephroma..	?	

<div align="center">

Tumors of the Renal Pelvis and Ureter
Similar to tumors of the bladder

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This classification retains the old term "hypernephroma," limited, how-
ever, to tumors which have originated from adrenal rests, just as tumors
from adrenal rests may arise elsewhere.   The most frequent benign tumor
is a simple adenoma which is potentially malignant; it is not seen very often
and is likely to be so well encapsulated that it can be enucleated readily,
leaving the normal part of the kidney.   In most cases, however, it is better
to remove the kidney, provided the opposite kidney is healthy.   The com-
mon tumor of the kidney is a carcinoma which arises from the tissue of
the kidney itself.   Such carcinomata probably comprise 80 per cent or
more of all tumors of the kidney.   They are malignant, not very radio-
sensitive, and have an average life history of between two and three years.

These tumors usually metastasize by way of the blood stream but they can metastasize by invasion, and occasionally spread into the abdomen by means of the lymphatics. Benign connective tissue tumors of the kidney are rare, but a sarcomatous type of mixed tumor occurs. These mixed tumors make up about 12 per cent of all tumors of the kidney. The embryonal tumors are found mostly in children, new-born and infants. The tumor popularly known as the Wilms's tumor is radiosensitive, though not radiocurable, and one will see large tumors of this type in children shrink markedly under irradiation. At the end of the list is the rather questionable tumor which occasionally occurs as a true hypernephroma.

When the variability in the malignancy of these tumors is considered in relation to treatment, there can be no question in anyone's mind that an early diagnosis is extremely important. If we expect ever to cure a cancer of the kidney we must make an *early* diagnosis, before metastases have occurred, and perform nephrectomy in such a way that there will be no spread of the cancer cells at the time of operation.

Even recent statistics seem to show that the early diagnosis of cancer of the kidney has advanced very little though, with the advent of excretory urography, one would expect to be able to diagnose these tumors much earlier. The three cardinal symptoms are hematuria, pain, and palpation of a mass in the renal area. In the majority of cases all these symptoms are present when a diagnosis is completed and this is not an early diagnosis. In about 30 per cent the initial symptom is hematuria alone, and this offers an opportunity to make an early diagnosis. Again let me emphasize the importance of a thorough urologic examination at the first sign of blood in the urine. There are a great many causes of this symptom besides cancer, many of which are insignificant, but when blood is present an idea as to its origin should be had at once. Tumors may bleed only a few days, never longer than two weeks, and then not bleed again for months, so that the opportunity for an early diagnosis may be lost with the cessation of bleeding because of delay in making a complete examination at that time.

With respect to irradiation as the treatment of choice for the average tumor of the kidney, except Wilms's tumor, I think the same criteria apply as for tumors of the rest of the urogenital tract. With a definite diagnosis of tumor of the kidney in an adult, irradiation previous to nephrectomy may be of some benefit if it is a large tumor, because often there will be enough shrinkage to make the nephrectomy easier. But to subject these patients to irradiation alone is not recognized as the proper treatment of tumors of the kidney. On the other hand, if metastases have occurred, one would rarely be justified in attempting nephrectomy because there would be no chance of curing the patient. Occasionally there is profuse bleeding from the kidney repeatedly enough to cause secondary anemia. In such a case nephrectomy would be a palliative procedure, and not radical

surgery. Radical surgery, of course, should not be attempted for a tumor of the kidney in which metastases have occurred.

With reference to statistics, a series of cases showing five-year cures of tumor of the kidney would be of considerable value because the life history of these tumors is usually short—patients rarely surviving more than from two to three years. All those living beyond five years would be reasonably certain to have been cured of cancer of the kidney.

Tumors of the renal pelvis and ureter are similar pathologically to tumors which occur in the bladder, which will be discussed next. The surgery of tumors of the renal pelvis is limited to one procedure, namely, the radical one of nephrectomy and ureterectomy. When a definite diagnosis is made of tumor of the renal pelvis, nephrectomy and ureterectomy are in order. There is no other procedure which will cure the patient. If a simple nephrectomy alone is done, the tumor probably will recur in the ureter because of previous extension. Whether one removes a cuff of the bladder at the point where the ureter opens into it is a matter of choice, but the whole ureter should be removed down to the bladder. Of course, if the cystoscopic study shows that there is invasion at the orifice, one should remove a cuff of the bladder along with the ureter, so that the operation would be radical nephro-ureterectomy and removal of a cuff of the bladder with the ureter.

Tumors of the bladder form a chapter which is in utmost confusion. No uniformity of opinion exists amongst urologists as to the proper line of treatment. The members of one group advocate purely palliative and conservative treatment. Many of them probably believe that their conservative treatment is curing some of the patients. Another group still believes in operation for these patients. Members of this group are not so confident of the effect of irradiation. Naturally this difference of opinion has led to a great deal of confusion and it is very difficult for one to get any order out of this subject. Let us examine first the following classification of tumors of the bladder:

Tumors of the Bladder

Classification	Incidence	Average Life
Epithelial:		
Papillary	90%	
Papilloma		
Benign		
Malignant (single and multiple)		5–10 years
Carcinoma		3 years
Sessile	7%	
Adenoma (rare)		
Carcinoma		2 years
Scirrhous		
Squamous		
Adenocarcinoma		

Classification	Incidence	Average Life
Mesothelial:		
Sarcoma....	3%	1 year
Myxoma, myoma, fibroma		
Vascular tumors.......		
Heterotopic:		
Dermoid and teratoma		
Rhabdomyoma........		
Chondroma...........		
(Carcinogenetic):		
Aniline dyes..........		
Bilharzia......		

Almost every one is more or less agreed that there are two very distinct types of epithelial tumors of the bladder, namely the papillary and the sessile or infiltrating tumors. The papillary tumors are further divided into papillomata and papillary carcinomata. Papillomata are distinctly of two types; many are definitely benign in the early period of their life history and become malignant later. A great many authors group the benign and malignant papillomata as one type of tumor. Furthermore, papillomata may be single or multiple. In those instances in which they are multiple, there is a dispute at present as to whether this multiplicity is due to some common carcinogenetic substance, which primarily causes the tumors, and which may attack any part of the bladder wall, or whether the primary tumor has the ability of implanting itself. Of course, when the bladder fills and empties, different portions come into apposition and a papilloma at almost any point will be in contact with the wall opposite it, so that it could implant itself to different portions. When these tumors are multiple, however, they are usually confined to the region of one or the other ureteral orifice. Then there is the papillary carcinoma. The distinction between a malignant papilloma and a papillary carcinoma is that in the papilloma the malignancy is limited to the tumor itself; there is no infiltration at the base of the tumor, whereas, in the case of a papillary carcinoma, the cancer has infiltrated the wall of the bladder or the base of the tumor and is not confined to the tumor itself. Another difference between simple papillomata, whether they are benign or malignant, and the papillary carcinomata of the bladder is the fact that the papillomata will respond well to what is called fulguration or diathermy, or whatever you want to call the treatment introduced in 1912 by Edwin Beer of New York. Before this treatment was introduced very few tumors of the bladder were ever cured except by radical surgery because they almost invariably recurred when removed by the method of cystoscopic snare. These recurrences required repeated removal by the snare until the tumors became so malignant that the patient eventually died. Rarely was a patient cured by the snare treatment when a benign papilloma was removed radically. Nowadays most of these simple papillomata can be

cured by fulguration. Since these comprise such a large percentage of tumors of the bladder, more than half of all patients with such tumors can be cured by the simple measure of fulguration alone, if it is used early, consistently and thoroughly.

Fulguration does not react so favorably in the treatment of papillary carcinoma, the malignant cells of which have invaded the bladder wall. Usually at cystoscopy one can differentiate the papilloma, whether benign or malignant, in which the cancerous change is confined to the papillary structure, from the papillary carcinoma which has invaded the vesical wall. Cystoscopically, the wall at the base of the tumor is raised in papillary carcinoma. Occasionally, at cystoscopy, patients' bladders are filled with a big carcinomatous mass, so that it is impossible to see the base of the tumor. One often is uncertain as to whether or not the cancer has invaded the wall of the bladder. Fortunately fulguration is useful even for these patients with such huge papillomata, either benign or malignant, because, if the tumors are of this type, they will melt away almost like butter under fulguration and will almost completely disappear after one or two treatments. If, two or three weeks after treatment by fulguration, there is very little improvement in the cystoscopic appearance, one then suspects that he is dealing with a papillary carcinoma which has infiltrated the wall of the bladder, and there is no longer any excuse to continue treatment by simple fulguration. None of the sessile types of tumor will respond to fulguration, unless in rare instances one uses very intensive coagulation of the tumor after cystostomy and extensive diathermy.

Tumors other than of the epithelial type are very rare in the bladder. Occasionally definitely benign tumors of connective tissue occur and, very rarely, sarcoma has been found in the wall of the bladder. It is a simple matter to get a biopsy and have a microscopic diagnosis. In these cases one can use to great advantage the method of Broders, in which the tumor is graded as 1, 2, 3 or 4 according to the degree of malignancy. This is of extreme value in the selection of the treatment.

Tumors of the bladder are common and the question comes up as to so-called precancerous lesions in the bladder, lesions which would become malignant unless removed or treated. Leukoplakia is a fairly common lesion of this type. In some instances leukoplakic areas in the bladder have been watched and proved to become squamous cell carcinoma later on. Likewise irritation from a stone in the pelvis of the kidney can cause squamous cell formation—practically all cases of squamous cell cancer of the kidney have been associated with a stone in the pelvis. Another interesting aspect of tumors of the bladder is their appearance in men who work with aniline dyes. Experimentally, aniline dyes can produce tumor, and workers with aniline dyes frequently have tumors of the bladder. In almost all of these cases they are multiple papillomata. Ferguson of New York believes that tumors of the bladder form from some substance in the

system which stimulates this malignant change in the wall of the bladder. In most cases the change seems to start in the submucosa rather than in the mucosa. Apparently there is a substance which stimulates these tumors to form; aniline dye tumors are evidence of this fact. On the other hand, we know also that chronic irritation in the bladder is often an antecedent of a tumor, so that the subject is by no means solved. Another fact with respect to the implantation of tumors is that, with the opening of the bladder for resection, tumor cells implant themselves and start cancer wherever implanted. This would tend to disprove the occurrence of a carcinogenetic substance, at least in all cases of tumors of the bladder.

Upon consideration of the grades of malignancy of tumors of the bladder, we again find a subject in great confusion. As I have said already, the life-history of papillomata is prolonged. Benign papillomata, even though they are not treated, will not kill a patient in under ten or twelve years. On the other hand, the sessile type of tumor has a much shorter life-history and will kill patients within one or two years. The papillary carcinoma also has a relatively short life-history. The sarcoma is deadly and will kill in a very short time. In relation to the life-history of any tumor, its radiosensitivity must be considered. The papillomata and papillary carcinomata are the most radiosensitive of these tumors. All sessile tumors are more or less definitely radioresistant. Radium was used a great deal more five or ten years ago than it is today and one sees many patients who are miserable because of the inflammation caused by large amounts of radium previously used in the bladder. They have all sorts of urinary discomfort and complaints because of these radium burns. The lives of some of these people have been prolonged by this treatment. I think, however, that it should be considered more as a conservative line of treatment, a definite prolongation of life rather than as a cure.

Metastases, of course, occur from tumors of the bladder, just as from malignant tumors anywhere in the body. Such metastases may occur by invasion, by the lymphatics or by the blood stream. The lymphatics of the bladder are primarily pelvic and secondary to lymph glands along the large vessels, very much as in the lymph drainage from the testicle. When cancer cells from a tumor of the bladder have metastasized, a cure of the patient by any method of treatment is hopeless, except, of course, in the instance of a very radiocurable type of tumor in which the metastases themselves are discovered and caused to disappear by irradiation.

In the treatment of these tumors, one must consider whether to select fulguration, irradiation or radical surgery. There has been a tendency to compromise and use the palliative and conservative measures first, leaving radical surgery until it is found that these less radical procedures are not benefiting the patient. This is not a sound policy because it means that the radical surgery is done at an unfavorable period. If we are going to cure cancer of the bladder we should make up our minds at the time of

diagnosis what particular type of treatment is most likely to cure the patient. Those who believe that irradiation will cure, will treat their patients by irradiation; but there are a great many urologists in the country who do not believe that all cancers of the bladder can be definitely cured by irradiation. I am not speaking of the benign and malignant papillomata but of the sessile-type tumors which are radioresistant in most instances and which are not cured therefore by either radium or X-ray. When a diagnosis of this type of tumor is made one has to decide at once between resection or complete removal of the bladder, either of which procedures, of course, is radical. If the patient is 75 years old, for instance, one would not be justified in subjecting him to too great a risk because life expectancy is short but, if the patient is younger, it seems to me that it is logical at least to give this patient an opportunity to choose for himself, as nearly as he can from the facts which have been presented, between taking the risk of operation, and having simple palliative measures used. This brings up the question as to whether we should persist, as we almost always have, in keeping the facts from these patients. Most physicians are loath to tell patients that they have cancer. All feel it a duty to tell the relatives. This diagnosis should be confirmed by biopsy, of course, but with the proof of the diagnosis the question arises,—shall we tell the patient? This takes good judgment, because if there is no possibility of curing the patient it is just as well to let him go on in peace and ignorance and die of his cancer, but if a cure is possible by radical means, either you or I would want to know it and have the opportunity of choosing whether to take the risk of radical treatment or that of the more palliative and conservative measures. Radical surgery of tumors of the bladder just spoken of is not by any means satisfactory. When we come to resecting these tumors we find that they usually are very friable so that resections have not given good results, because implantations along the field of operation frequently occur. The only other radical procedure is total cystectomy, which requires previous diversion of the urinary stream. Ureters can be placed in the skin or the rectum, and, with perfection of the methods of uretero-intestinal implantation, many of these tumors can be treated safely in this manner. If the ureters are to be implanted into the rectum it should be done early, not after one has delayed for two or three years with the use of conservative measures. One should decide at the onset whether treatment is to be radical or conservative and not wait until it is too late for radical treatment to do any good.

Tumors of the Prostate

Frequency
Morbidity
Characteristics:
    Structural
        True glands
        Peri-urethral glands

Pathological
  Mixed varieties
  Primary lesions
  Mode of extension
    Invasion by growth
    Lymphatic spread
      Perineural
    Vascular spread
Clinical
  Life history
  Diagnosis
    Symptoms
    Palpation
    Cystoscopy
    Biopsy
      Needle
      Transurethral
      Perineal
  Treatment
    Palliative
    Conservative
    Radical

Tumor of the prostate is a very frequent type of cancer. Perhaps some of you saw in the papers an account recently of a bill presented in the senate, signed by ninety senators, proposing appropriation of a million dollars a year to be expended for research in cancer. The largest number of senators to sign any bill before is twenty, so that this is an almost unanimous endorsement by the senate of this bill for cancer research. This has its significance. These senators are of cancer age. They know of the huge number of deaths from cancer every year, and one of the frequent types of cancer in this august body is cancer of the prostate. Cancer of the prostate is more common than cancer of any other part of the body. It is estimated that one in every five men who have prostatism has a cancer of the prostate, and it is judged variously that from fifteen to thirty-five men in every hundred have prostatism. Cancer of the prostate has a very high mortality, although it shows great variability in malignancy, just as does cancer of the bladder. Sometimes it is slow-growing and the patient may live five or ten years. I remember quite distinctly a patient whom I saw when I first started practice who had a cancer of the prostate with extensive metastases; shot-like metastases were present in the lungs and typical metastatic changes of his long bones showed in the X-ray pictures. I know that that patient was alive eleven years later and had very few symptoms arising from this cancerous invasion. Such exceptions are hard to explain. I know also that the average life history is well under two or three years. Cancer of the prostate does not present as favorable an opportunity of microscopic diagnosis from which an estimation of its life history can be made as does cancer of the bladder. In

cancer of the prostate, a specimen can be obtained for biopsy with a needle through the perineum, or a specimen for microscopic study can be obtained from the vesical neck or urethra with the resectoscope. Cancer of the prostate invades by direct extension and its favorite manner of extension is into the seminal vesicles or above into the neck of the bladder. If, at the time of cystoscopy, one suspects the latter, one can easily resect a portion of the neck by the transurethral method and obtain a specimen for biopsy. The only other way to get a microscopic section in suspected cancer of the prostate is by surgical exposure through the perineum. Another problem with respect to cancer of the prostate is that there are two types of cancer. As you know, the prostate consists of five lobes which form the true prostate, but the portion of the prostate which undergoes hyperplasia or enlargement is a separate periurethral group of glands. In the majority of instances cancer apparently begins in the posterior lobe and extends into the other portions. It, however, can begin in the periurethral group of glands, after they have undergone hyperplasia, which usually comes on later in life and is probably related in some way to hormones. Recent studies by Hryntschak of over three hundred prostates, removed by suprapubic prostatectomy and carefully examined microscopically, showed definite cancer, unsuspected before operation, in 3 per cent of these hyperplastic lobes, and in some additional 7 per cent of the cases, very definite precancerous lesions were seen. In my own series of cases in which the prostate was removed through the perineum, malignant changes in the hyperplastic lobes were found in about the same proportion. It is evident, then, that primary cancer occurs in hyperplasia. These pathologic changes seem to be related to some type of chronic irritation. There was definite evidence of reparatory changes in the sections which Hryntschak studied; this he called a potential type of lesion which progressed into the precancerous lesion and later became cancer.

This brings us to a consideration of the treatment of cancer of the prostate. I think that the use of irradiation is very much in confusion. Just as in other types of urogenital cancer, many urologists believe that radium does not cure cancer of the prostate. On the other hand, the difficulty in the use of radical treatment for cancer of the prostate is that an early diagnosis is rare, in spite of the propaganda to educate the profession always to make a rectal examination whenever a physical examination is made. Osler said that the difference between a good doctor and a poor doctor is that a good doctor makes rectal examinations. We are not making early diagnoses in spite of this dictum, largely because many physicians discourage radical treatment of cancer of the prostate. Most urologists, I think, are perfectly satisfied to treat patients palliatively or conservatively and they do not attempt radical treatment. The only radical treatment is the removal of the cancer in toto before it has spread from its primary site of origin. Are we justified in making biopsies in all suspected

cases and, when positive, in attempting a cure, or should we continue to rely on palliative and conservative methods and never cure? One factor which has confused the issue has been the advent of transurethral resection. Many of these patients can be relieved of their urinary obstruction by transurethral resection, although they die of cancer. One can see how confusing the subject becomes unless definite reasons are given for one type of treatment or the other. If the patient is a man of 75, conservative and palliative measures are in order, since one is not justified, as a rule, in subjecting a man of this age to the risk of radical surgery. However, cancer occurs in younger men, between the ages of 55 and 65, who are in good physical health. Shall we tell these patients that they have cancer and that it is early and probably can be removed, or shall we keep it to ourselves and treat them conservatively and palliatively, knowing quite well that we are not going to cure them?

I shall discuss briefly *tumors of the testicles.* These are rare, and almost all tumors of the testes are malignant. One can recognize, I think, two large groups, one the so-called embryonal tumors and the other the adult tumors which are not embryonal. The embryonal tumors are also of two distinct types, namely, the mixed cell tumors and the monocellular tumors. The mixed cell tumors have long been known as teratomata and monocellular tumors were known for a long time as seminomata but more recently have been recognized as embryonal carcinomata. Now, curiously enough, these embryonal tumors produce a gonadotropic hormone which appears in the urine. A test can be made for this gonadotropic hormone in the urine and this test is of great help both in diagnosis and in prognosis. Chart 1 is one compiled in collaboration with Dr. Powell.

Chorionepithelioma, a mixed cell tumor, produces the largest amount of hormone in the urine. This type of tumor any place in the body, whether of testicular origin or not, will produce gonadotropic hormone. Among the monocellular tumors, the adenocarcinomata are less active in producing the hormone. The more embryonal they are, the more hormone is excreted. In other words, the more primitive tumors produce more hormone in the urine than the less primitive. On the other hand, the adult type of tumor with well differentiated cells, such as the adult teratomata and the adult seminomata, do not produce gonadotropic hormones. Under the microscope these adult tumors may closely resemble the more primitive types, so that, microscopically, one would not always be able to differentiate between them. In this regard, the test for gonadotropic hormone is of great value. From a practical standpoint, however, there is little to be gained by the differentiation, because all of the monocellular tumors, both the adult type (seminoma) and the embryonal types (monocellular carcinomata) are more or less radiosensitive. The teratomata or mixed tumors, however, are not very radiosensitive; mixed embryonal tumors show only a very slight response to irradiation and the adult type

of teratoma is definitely radioresistant. The point particularly to be made in this respect is to emphasize the value of an early diagnosis. In comparison with other urogenital tumors, it is simple to make an early diagnosis of a tumor of the testis. The patient notices first a lump in the scrotum and one of the chief characteristics of this lump is the sensation of weight which it gives. The next step is to test the urine for gonadotropic hormone. When one's suspicions are aroused clinically, by the history and by palpation, that the lump is a tumor of the testis, even

CHART 1

Analysis of 58 Patients with Testicular Tumors and Hormonal Tests

HISTOLOGICAL CLASSIFICATION	NUMBER OF CASES	HORMONAL EXCRETION *M.U.L. (AVERAGE)	RESPONSE TO IRRADIATION	PROGNOSIS
A. Embryonal tumors (hormone present):				
I. Teratoid (mixed-cell):				
a. Chorionepithelioma......	2	20,000 to 3,000,000	Fair	Poor
b. Adenocarcinoma.........	6	2,000 to 1,000,000	Fair	Poor
c. Differentiated (with carcinomatous elements)...	6	1,000 to 200,000	Fair	Poor
II. Carcinoma (monocellular):				
a. Primitive...............	7	1,000 to 1,000,000	Good	Poor
(1) Without lymphoid stroma...........				
(2) With lymphoid stroma...........				
b. Differentiated..........	26	1,000 to less	Good	Good
(1) With hormonal excretion...........				
(2) Without hormonal excretion.........				
B. Adult tumors (hormone absent):				
Adult teratoma................	3	None	Poor	Good
Adult seminoma................	8	None	Good	Fair
C. Miscellaneous tumors.............	0	None		

* Mouse units per liter of urine.

though the test of the urine for the hormone is negative, one is justified in performing orchidectomy at once. It is only by this procedure that many of these patients will be cured. If we could see these patients within a month after the first appearance of the lump and perform orchidectomy immediately, a very high percentage of them would be cured. Statistics show that the average time is six months or longer after onset before a diagnosis is made. During the time of study and investigation there should be as little and as gentle handling of the testes as possible, because

squeezing and manipulation can easily cause metastasis. At the time of orchidectomy the cord should be immobilized and clamped before one attempts to manipulate the testes and scrotum at all. There should be no exploratory operations for tumor of the testes. I believe there is no excuse for delivering a testicle and cutting it open if operating for tumor. The surgeon should have his mind made up beforehand that he is going to remove the testicle. About the only mistake he could make would be to remove a gumma, and if the history, the blood and urine tests are negative, this error is unlikely. After the tumor has been removed in this way, careful microscopic studies can be made. It is the correlation of the microscopic study with a series of hormonal tests that enables one to make a prognosis. If an early diagnosis has been made and immediate orchidectomy performed before metastases have occurred, the patient will be cured. Subsequent hormonal tests will be negative. If these tests persist in being positive after orchidectomy, however, metastases have occurred. From the experience gained with irradiation recently, I hesitate to advise such a patient to have radical removal of the preaortic lymph nodes. I have done fourteen of these operations, have had no surgical deaths, and the results have been unusually good. At the same time, I am frank to admit that some of these patients might have been cured by simple orchidectomy. In only a few of these patients did the lymph nodes which were removed show metastases; in the others no tumor cells were found in the resected lymph nodes. The alternative form of treatment in these patients in whom the hormonal excretion persists after orchidectomy, is irradiation; this is the logical procedure when the microscopic study indicates a tumor which is definitely radiosensitive. If metastases have occurred, the probability is that they are beyond removal by surgical means. Metastases of the left testis occur primarily in the preaortic lymph zone; of the right testis, in the prevenacaval lymph zone and secondarily across from one side to the other. If one planned to resect the primary zone, the logical thing to do would be to take out the primary and secondary zones of both testicles. This would be extremely difficult to do, particularly on the left side. These cancers often spread rapidly from the primary lymph zones to the secondary zones, and the subclavicular lymph node of Virchow is not an infrequent site of secondary metastasis. I am inclined to believe, therefore, that the logical treatment for tumors of the testes with metastases is irradiation. I also believe, however, that we could cure a high percentage of these patients by orchidectomy without irradiation, if an early diagnosis were made. The only way we can make an early diagnosis is to suspect a lump in the testicle, which is heavy and gives the sensation of weight. Then do an immediate orchidectomy, even though the hormonal test is negative. In this way we will cure a great many of these patients.

RETROPERITONEAL PARARENAL OSTEOMA

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Retroperitoneal tumors are relatively uncommon in comparison with tumors occurring in other parts of the body. Articles dealing with this subject are generally concerned with the reporting of a single case, although in a few instances the author has been able to record more than one case. This type of article is the exception.

Goebel (1) reported three cases of retroperitoneal tumors and presented a very exhaustive review of the literature. He was able to collect a total of one hundred and one cases. More recently Schmid (2) tabulated a series of two hundred and sixty-seven cases. In all these tabulations, no case was found similar to the case I am about to report.

The finding of a retroperitoneal pararenal tumor composed of bone is an extremely unique experience and stimulates interest in the possible method of its origin.

CASE REPORT

Mrs. W., sixty-three, was referred by the late Dr. Donald P. Abbott. The patient first entered the Presbyterian Hospital on December 13, 1925. Her last admission was on February 23, 1934. Between these two periods she had twelve other admissions. During this time she was treated for spastic and fermentative colitis, diverticulitis and chronic diverticulosis of the colon.

There were no symptoms referable to the urinary tract at any time during the nine years she was under observation.

A routine roentgen-ray examination of the urinary tract was made at the time of the first admission to the hospital. This showed a very dense shadow, sharply defined, slightly nodular in outline, approximately oval in shape and measuring 7.5 cm. in its longest diameter and 5 cm. in its widest. This shadow was in the upper part of the left side of the abdomen at the level of the first and second lumbar vertebrae with its long axis perpendicular to the spine, its outer tip overlying the eleventh and twelfth ribs. The mesial margin of this density lay 3 mm. from the tip of the left transverse process of the first lumbar vertebra.

On lateral view this shadow overlies the body of the second lumbar vertebra, covering the posterior two-thirds of this vertebra and spinal canal backward to the base of the spinous process. In this projection this shadow measured 5 by 5.5 cm.

During the nine years that she was under observation repeated blood Wassermann tests were all negative and several basal metabolic rate determinations were always within normal limits.

Many urinary examinations were made on each of her fourteen admissions to the hospital and they were all negative.

Table 1 gives the various blood chemistry examinations.

A cystoscopic examination was done on May 14, 1927. The bladder was normal, the ureters were catheterized without difficulty or obstruction. The urines from the right and left kidneys, as well as from the bladder, were free of pus, negative with Gram's stain, sterile on culture. Smears for tubercle bacilli were negative, as were guinea-pig inoculations for evidence of tuberculosis. Subsequent examinations for tubercle bacilli were also negative.

A set of retrograde pyelograms were made and they were normal. A shift film with a shadowgraph catheter in place was made, and this showed that the large shadow maintained the same relationship to the tip of the left ureteral catheter before and after the shift.

TABLE 1

DATE	SERUM Ca	SERUM P	UREA N	URIC ACID	CREATI- NINE	N.P.N.	CO_2 VOL. %	SUGAR	Cl AS Na Cl
4/ 2/26			16.8	3.9	1.3	38.3	40.0	108.1	515
5/14/27			16.2	4.9	1.3	33.5	64.5	90.9	514
11/27/28			19.0	5.7	1.7	36.5	59.8	89.7	455
8/ 9/29			22.7	5.7	1.8	36.3	60.7	131.6	493
1/16/30			20.0	5.3	1.4	43.2	65.5	104.7	484
2/28/34	12.6	6.1	14.8	5.7	1.4	33.3	61.4	95.2	530

Note: All readings are mg. per 100 c.c. except for the CO_2.

Several sets of intravenous pyelograms were made at various times during her stay in the hospital, and they were all negative and gave no additional information. Because of the fact that there were no symptoms referable to this shadow, because of the negative character of the urological findings, and because the shadow was found on routine examination and did not increase in size over a period of nine years, operation was not advised.

The problem of determining the actual location and nature of the shadow-producing body proved interesting and difficult; the location of the shadow was readily determined but its nature was not. The conclusion was reached that the shadow was not due to a stone in the kidney, but that it was extra-renal, and that it lay in, or practically in, the same body plane as the kidney, and that it was either attached to, or was just below, the lower pole of the kidney.

The conclusion was based on the following facts: 1. In a shift film made with a catheter in the ureter there was no change in the relation-

ship between the catheter and the shadow; 2. In shift films made with both retrograde as well as intravenous pyelograms, there was no change in the relationship between the shadow and the pyelograms; 3. A lateral film showed the shadow over the spine.

The possibility of calcification in a cyst attached to the lower pole of the kidney was given due consideration—but was eliminated because of the very dense nature of the shadow.

The patient's last admission to the hospital was on February 23, 1934, at which time a diagnosis of acute diverticulitis was made. A colostomy was performed by Dr. Vernon C. David on March 14, 1934, and the patient died six says later, on March 20, 1934.

The *autopsy* was performed by Dr. Carl Apfelbach and the anatomical findings were: diverticulitis of the sigmoid portion of the colon; partial obstruction of the colon; spontaneous rupture of two diverticula; acute fibrinopurulent peritonitis; thrombophlebitis of the inferior mesenteric vein; slight jaundice, recent colostomy; acute retrogressive changes of the myocardium, liver and kidneys, chiefly cloudy swelling; erosion of the lining of the esophagus by vomitus; aspirated vomitus in the bronchial tree; extensive hemorrhages of the lungs; diminution of lipoid material of the adrenal cortices; generalized arteriosclerosis; calcified left peri-renal mass (osteoma); cystitis cystica; varicose veins of the lining of the urinary bladder; adenomas of the liver; redundant transverse portion of the colon; partially obliterated left internal iliac vein; chronic indurative aortic endocarditis.

Gross description: At the level of the upper pole of the left kidney, and between the kidney and the spine, inferior to the adrenal gland, there is a hard, oval mass with maximum length of 6.5 cm. and a maximum width of 4.8 cm. There is a fibrous capsule less than 1 mm. thick attached to the underlying bone. This capsule is embedded in the surrounding perirenal adipose tissue. The only connection between the mass and the vascular system is through a minute vein about 1 mm. in diameter, that extends to the renal vein, and there are no attachments between this mass and any of the surrounding structures. The surface is irregularly nodular. The mass is split through its largest plane. The inferior two-thirds are composed of uniform grayish-brown bone, in which there are only a few red regions representing small blood-vessels. At the superior end of the mass there is also bone, but this contains many more minute spaces of reddish-brown tissue resembling marrow. The compact portion of the mass cuts with great resistance, being firmer than the compact bone elsewhere in the body. The mass weighs 105 gm.

Histology. In sections through the inferior portion of the bony mass there are only occasional cancellous portions. The remainder is made up of compact bone with fairly well formed haversian canals. The bony structure is mature.

In a section through the superior portion there are a number of spaces in which there is myeloid tissue with a few islands of granulopoiesis and erythropoiesis.

The finding of a retroperitoneal pararenal osteoma naturally arouses our interest in the question of its possible method of origin. When considering the origin of this tumor, it is necessary to make a sharp differentiation between pure osteoma and cases of retroperitoneal pararenal new growth, in which bone formation has been found.

A case belonging to this latter category was recently reported by Hansmann and Budd(3). One of their cases showed extensive bone formation in a tumor, the structure of which resembled the adrenal gland. In my case, the tumor was composed only of one kind of tissue, namely, bone.

Ewing (4) observes that in dealing with a circumscribed overgrowth of bone "the distinctions between inflammatory and neoplastic hyperplasia of the tissue are often so obscure that it has never been possible to define exactly the limits of osteoma. True progressive neoplasms, which adhere to Virchow's criteria and in which bone is the essential and not the secondary or accidental product, are not common, but chronic processes which result in bone formation from trauma, inflammation and disturbance of nutrition are numerous."

Ewing adds that "even in cases in which the neoplastic qualities are least prominent (such as bone formation in necrotic tissue in the brain, eye, kidney or aorta; in the floors of ulcer; in the course of syphilis or tuberculosis) the size of the resulting bony mass, the long duration of the process and its eventful independence of the original exciting factor, occasionally there is revealed definite neoplastic characteristics." According to Ewing, histological study fails, as a rule, to distinguish simple hyperplastic overgrowth of bone from true osteomas. When the growth of bone is located in tissue other than bone it is termed heteroplastic.

HETEROPLASTIC BONE FORMATION

Ewing states that "in heteroplastic bone formation the process begins either in a cartilageuous or a fibrous matrix. The cartilage becomes more vascular and ossification occurs about the small vessels through the activity of the osteoblasts. In connective tissue the stroma becomes hyaline, calcification occurs under the influence of the osteoblasts with the appearance of osteoid and finally osseous tissue. Here one must conclude that the process is metaplastic, the fibroblasts acquiring the function of osteoblasts."

Ewing lists the following as factors which may be regarded as tending to call forth osteoblastic properties in fibroblasts:—

1. *Proximity to bone.* . (Certain authors assume that bone formation always results from osteoblasts which have wandered out from the peri-

osteum.)   Ewing notes that this theory finds a certain support in myositis ossificans, in which disease the process begins in the periosteum.

2. *Presence of calcified deposits.*   These figure in many instances of ossification of necrotic tissue.

3. *An active productive inflammation with organization of dead tissue and blood clot.*

4. *A special predisposition to calcification and ossification,* possibly connected with a disturbance of calcium metabolism, must be assumed to exist in such cases as reticulated osteoma of the lung.

Woolley (5) states that there are three hypotheses to account for heteroplastic bone formation: —

1. The occurrence of embryonic "rests" of osteogenic tissue, misplaced during development, which in later years, under stimulus of changed physiologic conditions, commence to grow and to produce bone.

2. A second theory postulates the transference of osteoblastic cells by way of the blood stream, so that they arrive in unusual situations where they lodge (embolism) and grow, producing bone.

3. The third theory, making use of the doctrine of metaplasia, holds that any cells may, within certain tentative conditions, change their morphologic features and become physically and perhaps chemically similar to other cells arising from the same general layer.

Woolley feels that, of these theories, that of metaplasia is the outstanding one.   He says that of the doctrine which "postulates embryonic rests there is no proof, save perhaps in rarest instances and in teratomata. There is no evidence that such remains play any part in the production of heteroplastic bone in any of the usual cases."   He adds "that it seems to us that the logical explanation of practically all osseous heteroplasia can be found in the doctrine of metaplasia.   Metaplasia, it seems, being a physiologic process of the widest possible application, must be also a process occurring under pathologic conditions.   The tissues of the body are formed by gradually changing steps that appear in response to physical and chemical conditions.   There is no intrinsic embryologic difference between the cells which are to form fibrous tissues and those which are to form bone.   The variations which arise are the results of physical and chemical differences in the environment of the cells which make it necessary that different structures be produced, and of the two orders of environmental factors, the chemical is more important.

The author continues that it is not known how the necessary chemical conditions favoring osseous metaplasia are brought about.   He says that E. R. LeCount (6) suggested that the presence of free blood plays a part in an unknown way; an interesting fact here being, that heteroplastic bone is most frequently associated with trauma and with inflammatory changes, which are, in turn, associated with hemorrhage.   Woolley suggests that it is possible that the presence of red blood cells which are

colloids of a certain concentration and composition, furnish the proper physico-chemical basis for deposition of salts in such concentrations that mesoblastic cells during the growth associated with organization are impelled in the direction of bone formation rather than towards fibrous tissue production.

Mallory (7) notes that the occurrence in soft tissues of tumor, that is, masses containing bone and cartilage, has been recognized since the time of Rokitansky. The origin of such tumors has been the subject of a great deal of study, and Mallory states that the following three theories appear to be worthy of consideration:

1. *The neoplastic origin* of these tumors is one which Mallory feels should be discarded except in certain frankly malignant cases.

2. *Origin from periosteum*, Mallory says, may be used to explain certain types of ossification of tendons, usually described as spur formation, and periosteal displacement may explain the so-called myositis ossificans. This origin, however, does not apply generally.

3. *Metaplasia.* The origin by metaplasia from fibrous connective tissue was first suggested by Virchow. Mallory notes that Virchow believed that all bone and cartilage—both normal and abnormal—arose by metaplasia from fibroblastic elements. Virchow regarded osteoblasts and chrondroblasts as modified fibroblasts. This doctrine of metaplasia in regard to bone and cartilage formation has been championed by Leriche and Policard to the extent that they regard osteosarcomas merely as fibro-sarcomas, passively ossified by the local condition of their environment.

Mallory summarizes his own opinion as follows: "Not only does metaplasia offer a simple and satisfactory explanation for the ossification of muscles, tendons, and ligaments, but it appears to be the only possible explanation of the many other types of heterotrophic bone formation constantly met by the pathologist, such as ossification of arteries, heart valves, pericardium and pleura, of absolute tuberculous foci, or of the falx cerebri, to mention only the commoner types."

Mallory concludes that many apparent bone and cartilage-containing tumors of soft parts are in reality of metaplastic rather than neoplastic origin. He also concludes that certain bone-forming spindle-cell sarcomas of soft parts may be more logically regarded as fibro-sarcomas with a metaplastic foci of osteogenesis than as true osteoblastomas.

Haining and Poole (8) report a case of "osteoblastome of the kidney, histologically identical with osteogenic sarcoma." They mention the periosteal, neoplastic and metaplastic theories of origin of bone occurring in soft tissues. They favor the latter theory and state that "the metaplastic theory of osteogenesis does violence to none of the ascertained facts and offers a rational explanation of the normal and abnormal production of bone." They are of the opinion that it is the only available

explanation for the type of extra-skeletal ossification which occurred in their case of renal tumor.

Haining and Poole note the rarity of bone-forming tumor of the kidney which they think is somewhat surprising in view of the apparent availability of calcium in the urogenital system and "especially in view of the numerous experimental demonstrations of a peculiar osteogenic proclivity in some of the urogenital tissue".

In the light of our present knowledge, and after reviewing the theories presented by various authors, previously quoted in this paper, the origin of this tumor may be discussed under the following headings:

1. That this tumor might be the end-result of the organization of an inflammatory process in the pararenal area, or, it might be the end-result of the organization of a hemorrhage, the result of trauma. The history of the patient, as reported in this paper, furnished nothing to indicate that such an inflammatory process, or a hemorrhage, due to trauma, had ever existed.

2. The second theory that might be considered is the one that postulates the transference of osteoblastic cells by way of the blood-stream so that they arrive in unusual locations where they lodge (embolism), grow, and produce bone. This seems rather far-fetched in trying to explain the origin and location of the tumor under discussion.

3. A remote possibility, and one which would be difficult to demonstrate with certainty, is that the bony mass in this case might represent metaplastic bone formation in a fibrosed accessory kidney. Against this theory, one may mention the fact that no evidence was found at autopsy that this patient ever had an accessory kidney, or, to be more specific, no evidence of an accessory renal pelvis, ureter, or blood supply was found.

4. In view of the fact that there was found a very thin delicate strand of connective tissue containing delicate blood-vessels one is led to speculate on the possibility that the tumor arose from the renal capsule as a fibroma, grew downward, never lost its very thin connection with the kidney capsule, and subsequently underwent metaplasia resulting in the formation of an osteoma.

5. Still further along the line of metaplasia may be mentioned the possibility that the original tumor was a retroperitoneal fibroma or lipoma that underwent complete ossification.

6. It would appear reasonable to interpret the tumor described in this paper, as a simple mixed tumor, the result of the development of an embryonal rest.

Ewing states that the term "mixed tumor" is now confined to comparatively simple, chiefly embryonal growths, of purely local origin, resulting from the overgrowth of embryonal structures with or without displacement.

Ewing states further that most of the accepted forms of mixed tumors

do not contain derivatives of three germ-layers but are bidermal or monodermal.

In this case the origin would be monodermal, probably from the fibroblasts of the mesothelium of the urogenital fold.

In this connection Hansmann and Budd state: "The potency of mesothelium has been appreciated since it has been established that synovial and pleural tumor produce bone, fat, fibrous tissue, angiomatous tissue, and glandular tissue. We assume that this might account for many of the mixed tumors with no particular characteristics which will associate them with a more definite embryonal structure. Such tumors are found both within and without the adult genito-urinary organs."

In a recent communication, (9) Hansmann again emphasizes the fact that spontaneous new growths of bone, without evidence of previous injury to the surrounding tissue, occur in the pleura, the meninges, and in the retroperitoneal region. He says they attain a considerable size and he considers them as true neoplasm. He regards them as tumors of mesenchymal tissue that have taken on the function of bone formation without any obvious stimulus for their so doing, and he considers bone formation quite within the potency of a mesenchymal cell and does not consider them metaplastic.

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TRANSPLANTATION OF THE URETERS INTO THE RECTO-SIGMOID IN YOUNG CHILDREN AND INFANTS

A Preliminary Report

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The most frequent indication for transplantation of the ureters into the rectosigmoid in children is, of course, exstrophy of the urinary bladder. As this condition occurs about once in every thirty thousand births and as there are about two million births in the United States annually, about seventy cases should occur every year. Unlike some other deformities, no compensatory function is to be expected; on the contrary, as the child grows older the situation becomes worse for both the child and parents. In addition, the danger of damage to the kidneys increases with years.

At what age, then, should the correction of this deformity be undertaken? Formerly, we were of the opinion that we should wait until the child could be taught voluntary control of the anal sphincter, or after from three to five years of age. If the anal sphincter is intact, and its tonicity can be determined by inserting the finger into the rectum, we now believe that the earlier the ureters are transplanted, the less will be the danger of complications and the better the opportunities for the child to develop both physically and mentally. We know that very young children tolerate surgical procedures remarkably well, as attested by operations for cleft palate, harelip, clubfeet, pyloric stenosis, intussusception, etc. With these facts in mind, we have undertaken this procedure in children as young as three months of age. We now have transplanted the ureters into the rectosigmoid in five patients who were all under one year of age (Figs. 1 and 2). All of these children are alive and well and the parents are extremely grateful for the ease with which the children can be cared for and the lessened discomfort and irritation of the child.

Formerly, one of the causes of mortality was the danger of peritonitis. With proper preoperative preparation and improved operative technic, this risk has been practically eliminated. In most instances the operation is performed in two stages, the right ureter being transplanted at the first operation and in about ten days transplanting the left side. The exposed bladder mucosa can be removed at the time of the second operation if the patient is in good condition; otherwise it is done at a later time and a plastic operation is performed to correct the bladder deformity. We

have not, thus far, attempted an operation for the separation of the pubic bones which is always present.

Transplantation is done without the aid of any mechanical devices or ureteral catheters. This, we believe, is by far the best procedure. As a rule there is not much reaction to ureteral transplantation, but one of the complications which may occur and which must be borne in mind is that the child will often be very irritable as a result of the exposed bladder and may do a great deal of crying. As a result of this overexercise of the abdominal muscles, these muscles become unusually strong, the fascia is quite thin, and the danger of breaking down of the wound must be borne

FIG. 1.   FIG. 2.

FIG. 1. Photograph of baby four months of age taken nine days after the second operation, showing lines of incision and general condition of the patient.

FIG. 2. Photograph of baby nine months of age taken ten days after left uretero-sigmoidostomy and cysteetomy, showing lines of incision and general condition of the patient.

in mind when the closure is done. In our experience, we have had two cases where the wound has separated by breaking the sutures in the abdominal wall at about the tenth day. In no instance did this cause any serious complication, except for delaying the time of the second operation and prolonging the stay in the hospital. Latterly, we have been using a fine steel wire to approximate the fascia; however, this must not be drawn too tightly. The wire becomes encysted and keeps the fascia in approximation until the wound is solidly healed.

In babies as in adults it is important that a good Trendelenburg position be obtained so the intestines can be easily and completely packed away

from the field of operation. The anesthetic we use is ether. The child's body is carefully protected to maintain heat.

There are certain points in the technic of the operation which we think are worthy of consideration. One is the primary fixation of the proximal
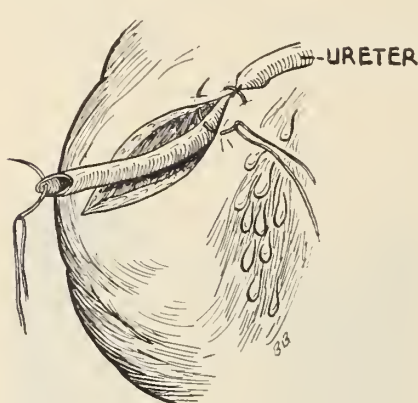
FIG. 3   FIG. 4

FIG. 3. First stage: Fixing of the proximal end of ureter
FIG. 4. Second stage: Further implantation of ureter between musculature and mucosa of gut
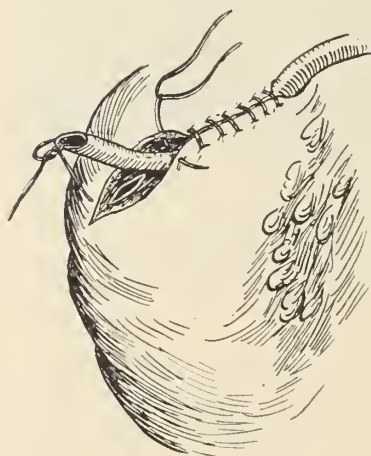
FIG. 5   FIG. 6

FIG. 5. Third stage: Additional fixation suture of the ureter and opening of mucosa
FIG. 6. Fourth stage: Implantation of ureter directly into gut
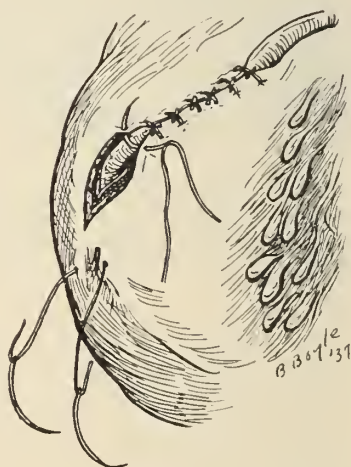
end of the ureter at the point of beginning the transplant (Fig. 3), then after submerging the ureter underneath the musculature (Fig. 4), it is again anchored about an inch from the free end (Fig. 5). In this way,

the ureter is steadied the entire length so that when it comes to introducing the free end into the gut, this part of the operation is much simplified (Fig. 6).

It is not easy to secure an intravenous pyelogram in these young children, but in only one of our cases were the ureters considerably dilated at the time of the transplantation; this did not materially interfere with the operative procedure.

As in all surgical procedures in the abdominal cavity, great care should be taken to protect the intestines and this is done by using warm saline packs to keep them out of the field of operation. The abdomen is completely closed without any drainage. Postoperatively, we keep a catheter or small tube in the rectum for a few days and at rather frequent intervals the bowel is gently irrigated with normal saline solution.

We do not know how long the upper urinary tract will remain free from infections. Patients previously operated upon whom we have observed over a period of years, occasionally developed a slight temperature and discomfort in the upper quadrant which is probably due to infection, but after a few days it generally subsides. We have one case—a patient then 8 years old—in whom the ureters were transplanted into the rectosigmoid eighteen years ago. She is now in good physical condition and has good kidney function. Of our past cases, a number of these patients are married and pregnancy has occurred in two instances.

From our experience thus far in this group of young children, we believe this operation should be done earlier than was formerly advocated.

THE MANUSCRIPTS, INCUNABULA AND EARLY BOOKS OF THE HYAMS COLLECTION IN THE BOSTON MEDICAL LIBRARY

WM. C. QUINBY, M.D.

[*Boston, Massachusetts*]

> Lo, and it was given unto man to know,
> And to heal the sick;
> But vouchsafed only unto the chosen.
> Bible.

The great importance of a knowledge of the history of medicine and of science as a foundation for a cultural estimate of the philosophical and spiritual trends of the present day has received especial emphasis in America during the years of the present century notably by the writings and collection of Osler—his Bibliotheca Prima—and by the brilliant leadership of Billings and of Garrison at the Library of the Surgeon General in Washington. A later recognition of this importance is found in the creation of professorships of the History of Medicine in several of our Universities, and still later the stupendous bibliographical compilation of Sarton's Introduction to the History of Science illustrates the great value of a study of all writings in their original source whenever possible, from the earliest date to the present.

A very important step in assembling such material for study was taken in June 1930 when the Boston Medical Library was the recipient from the Godfrey M. Hyams Trust of a sum of money to establish and maintain a collection of the writings of Jewish Medicine and Science to be named the "Solomon M. Hyams Collection." It was the desire of the founder of this trust that the collection be entirely comprehensive in its scope and embrace all material relating to Jewish Medicine in any language, including medical and allied books in Hebrew, together with medical writings of Jewish physicians from the earliest period to the present time. Search for important and great books and manuscripts of the past has resulted in the collection at present of about thirty-two medieval, renaissance and later manuscripts, twenty-eight incunabula of the fifteenth century, forty books of the sixteenth and seventeenth centuries, together with about one hundred and ten other volumes of later publication and over four thousand pamphlets.

Preceding the dawn of European medicine at centers such as Salernum the medical knowledge of the world lay chiefly in the hands of learned Jews many of whom in Hebrew and in Arabic had carried down the writings

of Hippocrates and especially of Galen, adding, as time went on, contributions of their own. Such knowledge was not available, however, to the European scholar till translations into Latin appeared, such as those of Constantinus Africanus (ob. 1087). Although reputed a man of great learning, nearly all of his writings were translations of the earlier works of the Egyptian Israelite known to medieval medicine as Isaac Judaeus (ob. 932 or 941). (Abu Jakub Ishak ben Soleiman el Israeli) A delightful account of this is by Charles Singer, "A Legend of Salerno: How Constantine the African brought the Art of Medicine to the Christians."* So even from the earliest beginnings, often in spite of cruelties and oppression, Jewish medicine and hygienic rules take high rank as we study the succeeding centuries.

As it becomes better known and still increases in scope, the Hyams Collection will be of great value as an aid to such study.

THE COLLECTION†

The sale of the library of Prince Dietrichstein, held at Luzern in 1933, provided the opportunity for procuring the well-known collection of nine manuscripts in Hebrew contained in that library. They are all of the fifteenth century. The total number of Hebrew manuscripts in the collection is twenty.

The Mafteah Harefuah of Elisha is the most complete copy known, as it lacks only one leaf in part two. This manuscript dates from the late fifteenth or early sixteenth centuries.

The Natan-ha-Meati translation of the Liber ad Almansorem of Rhazes, fifteenth century, is unknown in any other collection and is probably a unique copy.

Another very important Hebrew manuscript is an incomplete copy of the "Balsamo del corpo" of Natan ben Joel ben Palquera. Our manuscript consists of part three and fragments of parts two and four of the work, which is a complete treatise on medicine which was never published.

A most unusual Hebrew manuscript is an eighteenth century copy of the Lehem Tamid, a cabbalistic prayer book. It is very well illustrated in colors and encased in a fine binding.

The four manuscripts of the thirteenth century are all outstanding and worthy of special comment, as follows:

The Dietrichstein codex of the Viaticus of Constantinus Africanus on fine vellum and in a fifteenth century tooled binding is a magnificent example of the period.

* Johns Hopkins Hosp. Bull., 1917, xxviii, 64-69.
† The writer is deeply indebted to James F. Ballard, Director of the Boston Medical Library, whose extraordinary familiarity with the medical lore of the earliest days has made possible the creation of the Hyams Collection, for much information concerning it.

1. Title page of the Lehem Tamid. Ms. cabbalistic prayerbook of the eighteenth century of Italian origin. Beautifully illuminated

Cum priuilegio Pontificis maximi Leonis deci
mi: τ Francisci christianissimi Francorum regis.

Omnia opera ysaac in hoc volumine contenta: cum quibusdam alijs opusculis.

Liber de diffinitionibus.
Liber de elementis.
Liber dietaru vniuersaliu; cum cometo petri hispani.
Liber dietarum particularium: cum cometo eiusdem.
Liber de vrinis cum commento eiusdem.
Liber de febribus.
Pantechni decem libri theoricae: et decem practicae:

cum tractatu de gradibus medicinarum constantini.
Viaticum ysaac quod constantinus sibi attribuit.
Liber de oculis constantini.
Liber de stomacho constantini.
Liber virtutum de simplici medicina constantini.
Compendium megatechni Galeni a constantino com-
    positum.

Cum tabula et repertorio omnium operum et questionum in cõmentis contentarum.

3. Title page of Isaac Judaeus, Opera, Lyon, 1515

Ractatus Rabi Moyſi quē
domino & Magnificho Sol
dano babilonie tranſmiſit
Poſtquā admanus miniiſer
uitoris Moyſi iſrahelitici
cordubeni preceptum prin
cipis ac honorati regis peruenit cui deus
glorioſus honores augmentare dignetur
: quod mihi traſmiſit per quemdam ſuum
nuntium · ſ· ut ſibi ſcribere deberem re ,
gimen tale cui pſecurę & aſque dubitatio
ne aliqua poſſit decuris egritudinum que
nouiter ipſi meo dnō reuerendo ſuperuene
runt fideliter confidere · aquo deus digne
tur ipſas & oēs alias egritudines elongare
& ſanitatem perfectam cum eodem tempo
ribus uitę ſuę permanere · Mihi quidem ſi
gnificat dictus nuntius quod dominus me
us reuerendus cōqueritur de duritie ſeu ſic
citate ſuę naturę intātū quod nō pōt aſſel ,
lare niſi cū ſummo ſtudio & labore & quod
innouata ē et eidem melācolia & male cogi
tationes . & quod appetit eſſe ſolitarius &
timet mori : & quod debilitatus eſt ſtoma
cus eius taliter quod cibus corrūpitur ieo
abſque cōpleta digeſtione · Quare ſuperhis

4. First page of the Regimen sanitatis of Moses Maimonides, Florence, 1477

The complete vellum manuscript of the De proprietatibus rerum of Bartholomaeus Anglicus was written in Northern Spain about 1280 and came from the Spanish Monastery of Leyre in Navarre.

Two manuscripts of Isaac Judaeus are very fine and important items.

The fourteenth century is represented by the very beautiful Arabic manuscript of the complete Canon of Avicenna written in Persia in 1309.

A manuscript of outstanding importance is the "Privileges" of Ferdinand III, Grand Duke of Tuscany, dated at Florence, tenth of June 1593. It is a statute for the Jewish community of Pisa and Livorno, including among other privileges the right of Jewish physicians to practise their profession.

Dr. H. Kroner of Alberdorf in Wurtemberg, a great student of Maimonides, before his death completed a critical analysis of the known Arabic and Hebrew manuscript of the tract on "Poisoning and its Treatment". The complete manuscript came to the Hyams Collection from the widow of Dr. Kroner, through the kindness of Dr. Alexander Marx of New York.

The first medical book in Hebrew and the only one printed before 1500 is the Canon of Avicenna, translated by Joseph Lorki and Natan Hammeathi, and printed in five parts at Naples in 1491 by Azriel ben Josef of Gunzenhausen. It is exceptional to find Hebrew books in complete and good condition because of their extensive and hard use by scholars. The example in the Hyams Collection is a good working copy, complete, with the exception of a leaf of the table in book one. Leaf one of the text in this book is imperfect and the missing text is supplied in an early Hebrew hand. The leaves of the tables in the five books are in very poor condition.

Another very important book in Hebrew is the Commentary on the Pentateuch by Levi ben Gershon, Mantua, about 1475 to 1476. Levi ben Gershon, commonly known as Gersonides, 1288 to 1344, was a French physician, philosopher, mathematician, astronomer and exegete. This is his second work and, according to Haebler, is possibly the first book to be printed in Hebrew, even antedating the Pentateuch printed at Reggio in 1475. It was printed by Abraham ben Salomon Conat and Abraham Jedidijah de Colonia. Conat was a physician, Talmudist and printer. He set up a press at Mantua in 1475 from which he issued eight books up to 1480 when he suspended his business because of competition at Ferrara. Conat was proud of his work and used to accompany his name in the colophons of his books with the words, "Who writes with many pens without the help of miracles, for the spread of the Torch in Israel". The Hyams collection has an imperfect copy of this book.

Moses Maimonides, in Hebrew Moses ben Maimon, probably was the greatest Jewish physician of all time. He was often called the second Moses, or the Moses of his time. He was a Spanish-Jewish physician,

5. Last page of the Mishnah, Naples, 1492, showing signatures of three well-known censors

philosopher, theologian and astronomer, born in Cordova 1135, died in Cairo 1204. Maimonides is represented by first editions of his two printed medical books: the "Aphorismi medici", 1489; and the "De regimen sanitatis", 1477. The collection also has the first printing in Hebrew of the commentary of Maimonides on the Mishnah, 1492, which is also the first printing of the Mishnah. It is perfect and complete, with the signatures of three censors, and is the only complete copy in the United States.

Maimonides' influence was tremendous and far-reaching in space and time. It affected not only the Jews, but also the Christians, chiefly the Dominicans. This influence was important in itself, and also because until the eighteenth century Maimonides was the main channel through which Jewish thought reached the Gentiles. It can be strongly detected in Spinoza, and even in Kant (Sarton).

Jewish translators are represented by Faraj ben Salim and Abraham Judaeus of Tortosa. Faraj ben Salim or Moses Farachi or Faragut, was a Sicilian-Jewish physician and translator who flourished in the second half of the thirteenth century. He was employed by Charles of Anjou to translate medical works and became one of the greatest translators of his time. His principal and most important translation is the "El Continens" of Rhazes, which he completed in 1279. The "Continens" is the largest encyclopedia of Arabic medicine and the first edition (in the Hyams Collection) was printed at Brescia in 1486 by Johannes Britannicus.

Abraham ben Shem-Tob or Abraham Judaeus Tortuosenensis, son of a physician, flourished in Marseilles in the last of the thirteenth century. He studied medicine and wrote a short treatise on health. In collaboration with Simon Cordo of Genoa, he translated the "Liber de simplici", of Serapion the Younger, which we have in the extremely rare first edition, printed at Milan in 1473 and in the Serapion collection of Venice, 1497. He also translated the "Liber Servitoris" of Albucasis, one of the first medical books to be printed.

Johannes Hispalensis' translation of the "Secretum Secretorum" was published in 1477 with the "Conservatione sanitatis" of Benedictus de Nursia, under the title of "De regime sanitatis" and erroneously ascribed to Taddeus of Florence.

Abraham ben 'Ezra, a Spanish-Jewish philosopher, astrologer, and translator from the Arabic into Hebrew, wrote various books on mathematics and astrology, of which only two were printed separately before 1500: "De luminaribus et diebus criticis", Padua, 1482; and the "De nativitatibus", Venice, 1485. The latter is in the Hyams collection as well as a very fine edition, Rome, 1545, and the Venice, 1507, Opera containing all of his astrological writings.

Bonetus de Latis was a Jewish physician, astrologer, and rabbi. He wrote the "Anulus astronomicus", describing his astronomical ring, published at Rome in 1492 or 1493, which contains a woodcut said to be the first printed picture of a scientific instrument.

The very famous Simon of Trent case of 1475 is represented by three contemporary accounts of 1475 and 1476 of Dr. Johannes Tuberinus.

Dreams are considered of interest in the Bible but the only two interpreters mentioned by name are Joseph and Daniel. The "Expositio somniorum Danielis", (Memmingen, Albrecht Junne, ca. 1496) a pamphlet of eight leaves is very interesting and all editions are scarce because of the fugitive, ephemeral character of the publication. We also have an edition of 1515.

Some effort has been made to collect material on circumcision and the "Oratio circumcisionis", of Antonius Lollius, Rome, 1485 and of Bernardinus Carvajal, Rome, 1489, are rare and interesting pamphlets.

The "Repertorium morale" of Petrus Berchorius in three volumes, Nuremberg, 1499, a dictionary of the Bible; the "Pantheologia" of Rainarius de Pisis, in two enormous volumes; the "Sermones de adventu" of Robertus Caracciolus, Venice 1479 and Strassburg, 1485; and the "Sermones de tempore et de sanctis" of Peregrinus, Ulm, 1485, all contain important material on circumcision.

The great Jewish historian, Josephus Flavius, who flourished in the first century A.D., is important because of his history of the Jewish races from the creation to 86 A.D. It contains much of the medicine of the early Jews. We have the editions of Venice, Maufer, 1480 and Venice, Rubeus, 1486.

Bruno de Longburgo, an Italian surgeon, flourished at Padua about 1252. It is said that he was a Spanish Jew converted to Christianity. His principal work was his Chirurgia Magna which he later abridged under the title of Chirurgia Minor or Parva. The Chirurgia Magna was translated into Hebrew by Hilliel ben Samuel. Both his Chirurgia Magna and Parva are contained in the Collectio Chirurgica Veneta, commonly listed under Guido de Cauliaco, of 1499, which we have, as well as an edition in Italian from the Press of Simon de Luere in Venice, 1510.

Adamantius Sophista was a Jewish physician and Sophist who flourished at Alexandria in the first half of the fourth century. His treatise on "Physiognomy" is an epitome of Polemon's (second century, A.D.) treatise. The edition we have is the first, printed at Basel by R. Winter in 1544, and is the Latin translation of Janus Cornarius with the Greek text.

Amatus Lusitanus, 1511 to 1568, was a Portuguese-Jewish physician who practised at Ragusa and later at Salonica. We have editions of his "Cerationum Medicinalium" and of the "Apologia of Mathiolus".

Moyse Charas, a French-Jewish physician, lived from 1618 to 1698. We have his "Royal Pharmacopeia," Lyon, 1693, 1717 and 1753; and his "New Experiments on Vipers," Paris, 1672 and London, 1677.

Constantinus Africanus, the first great translator from the Arabic

המוהל מברך קודם החיתוך

ברוך אתה יי אלהינו מלך העולם
אשר קדשנו במצותיו וצונו
על המילה

אבי הבן מברך

ברוך אתה יי אלהינו מלך העולם
אשר קדשנו במצותיו וצונו
להכניסו בבריתו של אברהם אבינו

והקהל עונים

כשם שנכנס לברית · כן יכנס
לתורה ולחופה ולמעשים
טובים

6. Circumcision scene from the ms. register of Mohel Selig Gross

into Latin, lived in the eleventh century. He was the translator of the manuscript of Isaac Judaeus previously mentioned. His "Opera", Basel 1536, is a rare and important work.

Erra Pater, pseudonym for a Jewish physician who calls himself "A Jew, born in Jewry, doctor in astronomy and physick", is said to have been born in Bethany in Judea and wrote the very interesting and scarce tracts: "Prognostication forever", London, 1604; and the "Book of Knowledge", Suffield, 1799.

Garcia ab Orta, 1495 to 1570, was a native of Elvas but graduated from the Spanish universities of Alcala and Salamanca. He was appointed doctor to the King of Portugal, but in 1534 went to India where he remained until he died. He had a house and garden with many medicinal herbs at Goa. He published his "Coloquios des simples, e drogas he consas medicinais da India . . . , at Goa, in 1563. It contains chapters on fifty-seven drugs and simples, based on his personal observations. The original edition was the third book to be published in India and is extremely scarce because of its great contemporary popularity. We have a very fine copy of the first edition and also editions of Antwerp, 1567 and Venice, 1582.

Isaac Judaeus, a Jewish physician and philosopher, lived in the tenth century. Mention has been previously made of the two thirteenth century manuscripts. The "Opera" of Isaac, Lyon, 1515, is a very important and very scarce work. The "Medici Antiqui", Venice, 1594, a collection of Greek, Latin and Arab authors and the "De Febribus", Venice, 1576, a collection of classical authors on fevers, both contain treatises of Isaac Judaeus.

Johannes Hispalensis, a Spanish-Jewish translator from the Arabic into Latin, lived in the twelfth century. In addition to his "Regimen", 1477, translation of Aristotele's "Secretum" previously mentioned, the Collection has his rare "Epitome totius astrologiae . . ." , Nuremberg, 1548.

Jacob ben Samuel Mantino, an Italian-Jewish physician, flourished in the first half of the sixteenth century. He was an important man and in 1534 became physician to Pope Paul III. He translated philosophical and medical works, one of which was the fourth Fen of Avicenna's "Canon". We have the edition printed at Ettlingen, in the Black Forest, in 1531.

Meil Aldabi, or Meir ibn al-Dabi, wrote the "Schebile emuna" (Paths of Faith), an encyclopedia of science. In it will be found a section on the members of the body divided into three parts; the head, the inner members, and the outer members. He combined anatomy and physiology with therapy. We have editions of Amst., 1627 and 1708.

An important work of Moses Maimonides is the first edition of his letter to the Rabbis of Montpellier on astrology. It was translated

into Latin by John Isaac Levi and printed in Hebrew and Latin by Jacob Soter at Cologne in 1555.

Another interesting work is the "Porta Mosis" of Edward Pocock, the famous English Orientalist, printed at Oxford in 1655. His "Millot ha-Higgayon", Cremona 1566; the "Aphorismi", in Gradibus, Consiliorum, Venice 1514; and the "Constitutiones de fundamentis legis", Amst. 1638; and fifteen later works are in the Collection.

7. Bernardinus de Gordonio.   Shoshan ha-Refuah.   Paper and vellum ms.   Spain, 1468

Michael Nostradamus, the assumed name of Michele de Notre Dame, French astrologer and physician, of Jewish origin, lived from 1503 to 1566. His principal work was his "Centuries" in which he made his famous predictions of forthcoming events. We have two interesting editions of his "Prophesies", Lyon, 1605 and London, 1672.

The "Physica hebraea Rabbi Aben Tybbon" . . . was printed at Cologne

8. From the first edition of the Ma'aseh Tobiyyah, Venice, 1707

by Jacob Soter in 1555. Judah aben Tibbon is a pseudonym and the work is in Hebrew with the Latin translation of John Isaac Levi. Steinschneider places this "Physica" in the class of anonymous books and suggests that it was written by Jakob Antoli of Marseilles, who is known as a translator from the Arabic and worked as such at Naples in 1232.

Rodericus à Castro was a Portuguese-Jewish physician of the seventeenth century who wrote a well-known book on the diseases of women under the title "De universum muliebrium morborum medicina". In the collection is a copy of Venice, 1644 and also his "Tractatus de complexu morborum", Florence, 1624.

Rodericus à Fonseca, a Spanish-Jew of Lisbon, taught at Pisa and Padua in the seventeenth century. He wrote a number of medical works of which six are in the Hyams Collection.

Zacutus Lusitanus, a Spanish-Jewish physician, lived from 1575 to 1642. We have his "De medicorum principium historia", Cologne, 1629, Amsterdam, 1636, and "Praxis medica", Lyon, 1637.

Jacob ben Isaac Zahalon, an Italian physician and rabbi, was born at Rome in 1630 and died at Ferrara in 1693. He acquired a high reputation as a physician and Talmudist. He was the author of "Ozar-ha-Hayyim" (Treasury of Life), a medical work in thirteen parts, the last of which was left unpublished by lack of funds, published at Venice in 1683.

Worthy of particular mention are the following:—Juda Charisi, Likute ha-pardess, Venice, 1519; Johannes Draconites, Von Zwillungen in Rebeca Leibe, Lubeck, 1550; Johannes E. Nuremberg, Historiae naturae, (Natural History of the Bible), Antwerp, 1635; Gershon ben Soloman, "Gate of Heaven", Venice, 1547; Rafael Mirami, Compendiosa introduttione . . . della scienza de gli specchi, Ferrara, 1582; David de Pomis, Dittionario novo Hebraico, Venice, 1587; Venice, 1587; Seder Pitron Halomot, Venice, 1623; Philo Judaeus, Oeuvres, Paris, 1619; John Smith, King Solomon's portraiture of old age, London, 1666; Isaac Cardoso, Philosophia libera, Venice, 1673; Messahalah, De elementis, 1549.

Many books of the eighteenth and even the nineteenth centuries are very interesting and only a very few can be noted at this time.

Tobias Cohn, a Polish-Jewish physician, lived from 1652 to 1729. He was familiar with nine languages and wrote an encyclopedic work entitled "Ma'aseh Tobiyyah". We have the first edition, Venice, 1707, and the rare Jessnitz 1721 imprint. It is famous for its illustrations comparing the human body to a house.

Benedetto Frizzi (Benzion Raphael Kohen), an Italian-Jewish physician, was born in 1736 and died in 1864. He wrote many books on Jewish life and laws, on medicine, mathematics, music and the Talmud. His most important work is the "Dissertazione di polizia medica sui ritti e cerimonie del Pentateuco", a large work in six volumes on the Mosaic Law, published

at Cremona and Pavia, 1787 to 1790 and Leghorn, 1878 to 1880, and written in Italian. The work was issued in separate parts at different times and in different towns and is consequently hard to find in complete sets. We have five parts of the first edition and a complete set of the Leghorn editions.

Andreas Norellius' "Diatriba de anibus esu licitis", Uppsala, 1746, is an interesting book on slaughtery and sanitary laws of the Talmud relating thereto.

There is much material on medicine and science in the Bible and Talmud and on circumcision and laws of hygiene and slaughtering.

QUACKS AND QUACKERY

M. G. SEELIG, M.D.

[*Director of Research, Barnard Free Skin and Cancer Hospital, St. Louis*]

A few months ago a friend of mine, an unusually shrewd and astute lawyer, asked me to address a group of his friends on quackery. It seems that he himself had almost fallen for the blandishments of a cancer quack, and his first reaction to this experience was the very common pathological urge to serve and protect society. I readily assented to assume the rôle of protector, because ever since my first dip into medical history, these many years past, I have had more than a passing interest in irregular medical practice; it would be mere child's play, therefore, to prepare the desired lecture. I discovered, however, when I sat down to the task, that I had never systematized or consolidated the information that I had accumulated. Indeed, when I thumbed through my own handbooks and special monographs on medical history, I was wonder-struck by the bulk of the material devoted to cultism and quackery in my own library. I happened to mention to one of my historically minded colleagues that I was digging into the subject of charlatanism. So in a few days he drove up to my door with his automobile literally filled with his collection of books and pamphlets dealing with the subject. Thereupon, a presumably light labor of delight and fancy was instantly converted into an unanticipated heavy research. But this was to be a popular address; it should not be overburdened with erudition, nor stodgy-stiff with scholarship. What actually happened was that the problem dissipated itself in the invasive charm incident to reviewing an old acquaintanceship with many of my old rascally friends, the quacks of history. Indeed, what finally came out of the effort was an essay for popular consumption.

Even the most discursive essay should have a ground-plan. So what we shall do, first of all, is to set down, within strict limits, just what the phrase *Quacks and Quackery* shall connote. Having settled the question of terms, then we shall look into some of the leading personalities and episodes in the story of irregular medical practice; and finally we shall inquire into the general whys and wherefores, by taking a glance,—what the French call a *coup d'oeil*—at those aberrations of the mind and emotions without which subscription to quackery would be impossible.

The word quack is derived, of course, from the duck. The dictionaries all say that it comes from the modern Dutch word "*kwaken.*" Why from the Dutch instead of from the French, English, German, or even the Hindustani, is an unexplained mystery. From what all of us know of ducks,

it would seem, off hand, that they chirp the same in all lands, with no duckly notion of creating a favored nation clause for the Netherlands. We are also left in the dark as to why the highly onomatopoetic word "quack" has taken on the connotation of ignorant, boastful and fraudulent practice. We know, again on the authority of the dictionary, that such is the definition, but no philologist tells us why. It may be that the simple five letter word is so expressive of vacuousness that the word defines itself, or perhaps the waddling strut of pretentiousness of the fowl has lent color to his love call.

No story better illustrates the dictionary definition of quackery than does the one that I heard associated with the late Dr. Weir Mitchell. It seems that the famous Philadelphia neurologist was rusticating, incognito, in a small Pennsylvania village, at the same time that an itinerant eye-quack was holding forth for a spell and a spiel. One evening, in the village hotel lobby, the quack, in order to build up the next day's business, was retailing his prowess to an audience of gullible village rustics. Among other stories, he related how he had successfully removed a blind eye, scraped the back of it and then replanted it, restoring complete binocular vision to the patient. Weir Mitchell, whose identity was unsuspected, asked, unobtrusively and with feigned guile, "Isn't that a very difficult operation, doctor?" The quack admitted that it would be for any one less skilled than he. "May I ask" inquired Dr. Mitchell, "what anesthetic you used?" "Oh!" said the quack, "I could hardly explain that to you,— you wouldn't understand; but I can tell you that it's shaped something like a spoon."

In these days of popular psychologizing it becomes almost necessary for a physician expounding the subject of quackery, to demonstrate his own complete freedom from a subtle defense reaction that rests on guild loyalty. I furnish this evidence by way of saying most unequivocally that I have detected, during the course of the years, no small measure of quackery (cleverly disguised though it may have been) within the ranks of so-called regular medicine. I shall not discuss this phase of the subject, for the simple reason that such delinquencies appeal to me as disgraces to a noble guild and as individual fraudulency, rather than as a system, or, what we call today, a "racket." Likewise, I shall not label Christian Science, Mesmerism, or the various and almost multitudinous other forms of pure suggestion, faith and mental healing as fraudulent, boastful and dishonest. My unwillingness to group these cults under the head of quackery lies in my, call it, if you will, generous inclination to grant to the various founders a sincere belief in the power of suggestion, faith and mind over body. I have, on more than one occasion, permitted and even advised selected patients to lend themselves, body and soul, to some form of faith cure. In countless other instances, however, I have had to subdue my inner storm and rage as I contemplated the fact that comfort, and even life

itself, had been sacrificed, or pain pitilessly prolonged by the folly of these cultists. It ought to be made perfectly clear that a sincere believer in faith or suggestion or prayer or mind, is not *ipso facto* a quack, because he applies his belief in the field of medical practice. It is no less necessary, however, to make it equally clear that we must be careful to keep our minds in the channel of straight thinking on this subject of the therapeutic value of the psychological spiritualities involved in the various cult practices that we have mentioned. A digression for that purpose is made necessary by the bulk of the loose reasoning that is scattered through popular literature. Take, for example, Stephan Zweig's "Mental Healers," in which we find an unwarrantably explicit glorification of Mesmerism, and the implicit inference that the regular and orthodox practitioners of medicine have not yet learned the therapeutic potency of suggestion, assurance and faith. Why, even the brutes know the assuaging power of assurance and faith. Any one doubting this can confirm the fact, if ever the opportunity presents itself, by watching a mother-monkey soothe and caress her ailing baby with assuring strokes of her palm, as she snuggles the youngster to her breast; and the oldest of classical literature, in various languages, has countless references to the curative powers of faith and belief; no pathfinder Zweig was required to make that discovery. He could have much better busied himself with setting down the limitations of mind as a curative factor in disease. Try to conceive a Zweig or a Mary Baker Eddy, or a Coué, or any of their disciples, beatifically and successfully exorcising the demon of a jumping tooth-ache, for any moderate length of time without calling to his aid a properly qualified dentist. It is not mere caviling to insist that Zweig's failure to justify his thesis lies not in his stress on the power of mind over matter, but in his failure to recognize the differences between organic and functional disease. Suggestion may share with faith the power to move mountains, but even granting my own limited knowledge of engineering, I'm sure 'tis easier to move mountains than to cure, by simple prayer or faith, or deep hypnosis, an advanced cancer of the mouth or tongue or breast. Unaided faith or hope or belief or prayer in the treatment of such types of organic disease is the alpha of disaster.

With some reluctance I exclude osteopathy also from the realm of quackery, but I do nevertheless exclude it because it is beginning to lay more and more stress on the scientific fundamentals underlying disease. There is much evidence to support the contention that, just as homeopathy finally fused the larger proportion of her doctrines with the basic principles of scientific medicine, so also osteopathy is now in the process of doing the same thing.

The relationship between chiropractic and quackery is a different story. This school may not have been conceived in iniquity or born in sin, its adherents may not be motivated as exclusively by mercenary motives as

some of us are inclined to think; its methods of "adjustment," massage and passive movements may not be excluded from the field of rational therapeutic procedures; and yet, to sensitive nostrils there is a malodorous taint to a theory that makes nerve pinching the one, only and sole cause of disease. We might excuse adherence to the theory on the same basis that Dr. Samuel Johnson explained to his fair dinner partner his incorrect definition of *pastern*,—"Ignorance madam, pure ignorance"; but there is so much boasting about this scientifically inadequate theory and there is so much more than a suspicion of fraudulency in the claims of so many individual chiropractic practitioners, that the combination of ignorance, boastfulness and fraudulency seems automatically to set the stamp of quackery on the school.

With the field cleared of the tangle of faith and mental healers, and with the schools of spinal adjustment out of the way, we may proceed to a discussion of the so-called essential quacks in medical history. Of necessity, one has to be selective and discriminating, for the woods are literally full of them. There are the quacks of ancient times and those of subsequent ages, quacks of the various nations, astrological quacks, mountebank quacks, women quacks, scurvy quacks, cancer quacks, beauty quacks, rejuvenation quacks, elixir of youth quacks, bone-setting quacks, artist quacks, dancing master quacks, and so on, almost *ad infinitum*. Surely, from such a banquet of East wind one must select with discrimination, else interest would be transformed into tedium. It is really a dull and stupid business to observe the monotonous similarity of the methods employed by the entire outfit; always the same type of appeal, with only such alterations in pattern or fringe as to mirror the variations in ingenuity of the individual rogues. So what we shall do is merely to sketch in some of the high lights in the chapter of essential quackery.

Scratch a Russian, they tell us, and you will find a Tartar. Just so, if you explore, however superficially, a Cagliostro or a Perkins, or an A-brams, or a Sir William Read, you will find all the attributes of a shrewd, conscienceless, intuitive master of human psychology. I think all of us will admit this. We might even grant that we also understand how these knaves secure victims. What all of us balk at is the admission that it is conceivable that any of us, individually, could fall for these methods. Shame tends to cloak our consciences. But I, for one, feel reasonably sure that if scientific medicine had exhausted all her resources in vain attempts to rid me of my pain, or at least to ameliorate it, I might readily accept a method of cure or of practice that I knew to be bizarre, or even scientifically irrational, provided some sufficiently plausible person painted the right picture for me. If everyone knew pain as the physician knows it,— wholesale,—or if people knew, as the physicians do, the psychic fears and dreads, frights, flights and despairs of the ailing, then they would know the truth of Barnum's famous maxim about the suckers. Barnum descended

to the language of the street, when he said, "There's a sucker born every minute." Dr. Llewellys Barker, the polished clinician of Johns Hopkins University, expressed the same thought in choicer phrase, when he said that, "Quackery forms a part of the want gratifying mechanism, which society financially rewards."

Society distributed these financial rewards to unworthy practitioners of medicine before and after the days of early Greece, when the temple priest-physicians purloined precious tokens from guilelessly trusting patients. And Society continues distributing them today. The story of the diamond necklace is well known. The older Dumas version of it and the more recent recountal by Stephan Zweig, in his *Marie Antoinette*, have been so widely read that it is reasonable to assume that almost every one is familiar with the rôle played by Cagliostro, the wily go-between in the execution of that historic scandal. What every body does not remember is that this same Cagliostro was one of the arch quacks in history. About two decades ago, one W. R. H. Trowbridge wrote a fat volume defending Cagliostro, but the defense does not ring true, for Trowbridge does not satisfactorily explain away the facts that the rapscalion he defends sold to both nobles and commoners all over Europe his famous elixir of life; that he concocted and sold a cathartic tea, designated by him as *"Lebensthee,"* the tea of life; that he sold beds guaranteed to provide painless childbirth, and chairs that cured rheumatism. Mind you, this all happened in the eighteenth, the so-called century of enlightenment. The medical historian, Baas, was nearer the truth when he said that this hundred years was a period during which superstition belonged to the noble passions.

In England about this same time there was a tailor, named William Read, who decided to set himself up as an eye specialist. He procured a "ghost writer" to prepare for him a treatise on eye diseases, and then he hired an impecunious poet to praise his name in verse. His next step was to quack his professional qualifications so assiduously and so unintermittently that they reached the ears of Queen Anne, whose bad eyesight made her an easy dupe for impostors, and who knighted Read for his skill. England was at this time fairly flooded with quack remedies of all kinds, —essences for headaches, liquid sweat, dropsy purging powders, and pastes for piles and fistulae. Among the crew exploiting these remedies there were several notorious women, not the least well known of whom was the widow Drew, who advertised herself as preparing and administering medicines for all her sex. In one of her advertisements, after emphasizing the fact that many hundreds of virgins had enjoyed the benefits of her pills, she adds, with quaint and appealing innocence, that she also has for sale all sorts of childrens' coats, wholesale and retail. Another English woman quack was Agnodice, the woman physician, who advertised her tincture for fits, powder for green sickness, pill for dry cough, diet-drink for scrofula,

infusion for ague, powder for purging, water for sore eyes, elixir for gravel, and numerous other medicaments. A bold, clever, resourceful and charmingly insinuating woman this Agnodice must have been. One of her advertisements reads,—"To my own sex I cure all diseases and accidents. If Venus should, unfortunately, be wounded by a scorpenious poison, by tampering with fiery Mars, it is then that I bring relief and comfort, and, by my antidotes, expel the poison, Jove-like, though never so far gone." The lady, evidently had much faith in the old Latin maxim: "*Verbum sapienti satis est.*"

There is little need to elaborate the theorem that quackery is universal. What we have pictured in eighteenth century England went on in all the continental countries during that same period, just as it had been going on in previous and has continued during subsequent eras. One French medical fakir, Ailhaud, is credited by the historian Garrison with having earned the infamy of destroying more lives than were lost in the Napoleonic campaigns. The spirit of Johann Andreas Eisenbart, arch medical impostor of Germany, and, as it happens, also an eighteenth century product, was caught in the amber of a German university student song:

"Kann machen dass die Blinden gehen
Und dass die Lahmen wieder sehen
Wida, wida, wit, boom, boom"

There's quackery for you, etched in with the quintessential acid of humor, restoring locomotion to the blind and sight to the lame!

One of the earliest American charlatans was Elisha Perkins, a Yale man, and, for a while, a much respected practitioner of Connecticut. He was active in the late 1790's. Electricity was in those days much more of a mystery than it is today. Perkins, riding the wave of interest in electricity created by Benjamin Franklin, constructed what we know today as an electric couple, a simple rod, made up of two different metals. These rods were stamped with the label, "Perkins' Patent Tractors." They cost twenty-five cents to make and sold for twenty-five dollars. These tractors were drawn (always downwards) over the diseased area. The diseases amenable to cure by their use were legion, and the application of the tractors assured a complete restitution to health. Medical men and medical institutions accepted the new cure-all as a gift from the gods. Congress was taken by storm; George Washington bought a pair and a Congressman from Virginia sold his plantation and accepted his pay in tractors. After a comparatively short time, the light dawned, as it inevitably and regularly does dawn. Perkins was expelled from the Connecticut Medical Society, and both he and his little rods were forgotten. Perkins was discredited in spite of the fact that he could have produced baskets full of testimonials. One clergyman wrote that the tractors had completely restored his health and that he had also found them useful in picking walnuts.

Now let us skip a whole century and come down to the gay American 1890's. I shall select one Albert Abrams to tell you about. Abrams was a San Francisco product, who, like Perkins, had enjoyed an exceptionally complete education, graduating from Heidelberg and serving later on the faculty of a leading medical school of San Francisco. He catapulted himself out of the company of honest physicians in the first instance by exploiting a method of spinal therapy, consisting in tapping the spinal column. He developed a school of spondylotherapy, in which he taught the highly intricate principles of his theory to students, at first for $50, and then later for $200 a course per pupil. Dr. Morris Fishbein is within the strict limit of truth when he says that the method was, in reality, not spondylotherapy, but spondulix therapy. At all events, within a reasonable time, about a decade, his method strayed off into the gloaming, there to die to the sweet strains of the choir invisible singing the eternal melody of Truth Unconquerable. Abrams, however, lived on to develop a new and marvellous method for diagnosticating disease, to-wit and as follows:— The patient submitted one drop of blood absorbed in a piece of filter paper. This drop of blood was placed on a so-called dynamizer connected up with dampners. The dampners were connected through an arrangement of wires, shunts, switches and leads, to the forehead of a person in normal health, who, during the test, must stand in a dim light, facing the west. Readings were then made from a rheostat and translated into an accurate diagnosis. After the diagnosis was established, a cure was induced by the use of another special machine known as an oscilloclast and costing the patient from $200 to $250. The chapter ends with the death of Abrams, in 1924, leaving behind him available assets of over a million dollars. Quite a while before his death, he had found a very valiant and enthusiastic supporter and propagandist in none other than Upton Sinclair, that high priest of the rights of the common people. One finds himself in a quandary whether to end this story with the Biblical quotation, "Lord, forgive them, they know not what they do," or on the lighter note of Shakespeare's Midsummers Night Dream, "Lord, what fools these mortals be."

The extent and depth of human gullibility is almost incredible. I can remember a few years back when a little machine, called an oxydonor, was sold in large numbers. It looked like a cylindrical, tin box, such as is used for dispensing talcum powder. A flexible wire was soldered to one end of it. When a gentleman retired for the night, he placed the contraption in a basin of water, under the bed, attaching the free end of the wire to his ankle. The apparatus was supposed to be an invigorator, particularly powerful in reestablishing virility. With full faith in the advertisements, one could retire at night a dejected, impotent, misanthrope, and awaken in the morning a potential Brigham Young.

We might consider the whole chapter of quackery to be as humorous

as is the incident of the oxydonor, were it not for the tragic consequences that are so frequently bound up with charlatanism. There is no need to go into detail. It may be accepted as a truth that cancer quackery alone, just a short chapter in the book of dishonest medical practice, holds within itself more of sadness, sorrow, pain and tragedy than even the most satanic Spanish inquisitor could have devised or dreamed of. I have no intention of preaching a moral; but it cannot be amiss to inquire for a moment into what I have already referred to as the whys and wherefores of quackery. Why do people have an instinctive faith in the miraculous? Why do they hearken to the touter? Why do they credit the irregular and discount the regular? Why, in short, do they permit hope to triumph over experience? Why does the merest flicker of pain so frequently start a train of emotions that runs down all the safety signals set by ordinarily sound judgment? The answer may be sought and it may also be found in two of the basic laws influencing human nature.

Firstly, man wants to be deceived. He hopes, always, to be shown the promised land, even though in reality it be only a mirage. Honestly wise physicians, as a rule, know this and they are willing to practice those inoffensive arts and wiles which may be justified by a fine conscience; when the interest of the patient and his well-being call clearly enough, they are willing to crook a bit the pregnant hinges of the knee of acquiescence, in deference to man's primitive desire to be cajoled.

The second of these two laws is that there is practically no extremity to which man will not go in order to conserve either his health or his life. Oliver Wendell Holmes, himself a physician, in one of his essays, says:

"There is nothing that men will not do, there is nothing that they have not done to recover their health and to save their lives. They have submitted to be half drowned in water and half choked with gases, to be buried up to their chins in earth, to be seared with hot irons, like galley slaves, to be crimped with knives like cod fish, to have needles thrust into their flesh and bonfires kindled on their skin, to swallow all sorts of abominations and to pay for all this as if to be singed and scalded were a costly privilege, as if blisters were a blessing and leeches a luxury."

After all, a successful quack is only a fine demonstration of the art of make-believe, just as his dupe rivals him as a genius in the art of believing. We ought not be very much wrought up over such a simple state of affairs. There is solace in comprehending the underlying psychological mechanism. There is even greater comfort in the thought that six or eight thousand years is a short time, in the biological sense, for the full development of conscience in man; a short while in which to allow him to slough his more or less inherent heritage of selfishness. Not only ships, but society also, must have her barnacles. Those of us who are wise learn to whistle as we scrape the hull of medicine.

A TECHNIC OF NEPHRECTOMY FOR TUBERCULOSIS

Designed to Prevent Tuberculosis of the Wound

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The indication for nephrectomy in subacute and chronic unilateral renal tuberculosis, in the absence of an active pulmonary process, rests securely upon the extensive clinical experience of many reliable observers. The most important prerequisites are the establishment of the diagnosis beyond reasonable doubt by means of the exact methods available to the competent urologist, and the demonstration of an adequately functioning uninfected kidney on the opposite side. In exceptional instances a minimal lesion of the opposite organ is not a contraindication. The pitfalls of making a false diagnosis of bilateral renal involvement have been frequently stressed, notably by Beer and Braasch.

The advisability of simultaneous subtotal removal of the diseased ureter (nephro-ureterectomy) has been debated often. The consensus of opinion inclines to the view that in the absence of stricture with dilatation and stasis above it, the removal of as much of the ureter as can be ablated through the lumbar incision is all that is necessary. When a stricture with stasis is present at or below the brim of the pelvis, nephro-ureterectomy is desirable. Thus Beer reported this procedure in only thirty-eight of two hundred and eighty-one cases.

One of the common and disagreeable sequelae of nephrectomy for tuberculosis is the relatively frequent tuberculous infection of the wound. This manifests itself either as infection of the sinus tract which has harbored a drain placed in the wound at the time of operation, or as a more or less general breaking down of the wound three to six weeks after operation. In the latter instances, primary union may appear to have taken place and even the drainage tract may have healed. Then redness and induration supervene and numerous discharging sinuses form, which lead down to the muscular layers through the subcutaneous fat either through the stitch holes or through numerous points in the linear scar itself. That the infection is tuberculous may readily be proven by bacteriologic methods, guinea pig inoculation, and histological examination of the granulation tissue. Such wounds may take six months to six years to heal despite liberal drainage, the use of antiseptics (iodine, iodoform, bismuth, mercurial compounds), heliotherapy (natural or artificial, local and general), roentgen-ray therapy, tuberculin and general hygienic measures.

The reports in the literature of the incidence of this complication attest its frequency and troublesome course. Braasch, in a study of two hundred and three cases, stated that in only 43 per cent had the wound healed within three months and that in only 87 per cent had the wound healed within a year. This statement indicates that 13 per cent took more than a year to heal. Beer, in a series of two hundred and eighty-one cases, reported sinuses or fistulae in 23.8 per cent. J. and W. Israel collected data concerning one thousand and twenty-three cases. In the first half year "fistula" was present in 29.4 per cent. Young had 18 per cent of the wounds break down in eighty-nine cases. Wildbolz reported "fistula" in 25 per cent of one hundred and seventy-five cases.

Various explanations have been offered for this high incidence of tuberculous wounds after nephrectomy for renal tuberculosis, and various details in the technic of the procedure have been evolved accordingly to reduce this incidence and possibly to eliminate its occurrence altogether. The earlier explanations attributed the complication to direct infection of the lumbar wound either during or after the operation. Thus it was believed that leaving a considerable portion of the ureter in situ, despite its double ligation and division with the cautery or the carbolized knife, led to the formation of a localized tuberculous process about the stump and subsequent involvement of the nearby recent wound. Therefore simultaneous subtotal removal of the ureter was suggested. In fourteen such procedures (nephro-ureterectomy) Braasch found no improvement in the end results. Beer, in thirty-eight cases, found the incidence identical with that group in which only a small part of the ureter had been removed. Israel and Young both recommended the injection of phenol into the distal ureter to accomplish destruction of the tuberculous mucosa and subsequent cicatricial fibrosis. Other surgeons (Binnie, Marion, Young) fearing the development of an abscess about the distal ureteral stump and subsequent perforation outward into the wound, have advised that the distal end of the ureter be fastened into the lower angle of the nephrectomy wound, subsequently treating the ureter by medicaments applied either through the resultant sinus tract or through a ureteral catheter introduced from the bladder by means of the cystoscope. It would seem that a more certain method of insuring a tuberculous fistula and tuberculous wound infection could not be devised. This procedure has been largely abandoned.

Albarran and Wildbolz, and many others, freed the ureter as far downward as possible and doubly ligated it. Protecting the wound carefully with packings the ureter was divided with cautery or phenolized scalpel, letting the distal end, after further carbolization, drop back and retract.

As it was generally believed that tuberculous wound infection was due to contamination at the time of operation, certain "do and don't" principles were adopted. Both Albarran and Israel recommended a liberal

incision so as to afford free access to the ureter and kidney. If the fatty capsule was adherent it was removed with the organ. Legueu thought the perirenal fat contained tuberculous foci. Gentleness in handling for fear of rupturing a distended calyx or renal pelvis, care in dividing the vascular pedicle lest the pelvis be incised, avoiding decapsulation, shunning exploratory nephrotomy—these were precautions to be observed. If the perirenal fat was not removed together with the organ, its removal before closure of the wound was advised.

Despite these admonitions and the observance of some or all the principles enunciated the incidence of wound tuberculosis was not altered. The occasional occurrence after nephrectomy for tuberculosis of a general miliary dissemination or a tuberculous meningitis suggested that tubercle bacilli were forced into the circulation by way of the renal vein in the course of the procedure. Beer in 1921 expressed the thought that this bacillemia was responsible for the wound infections appearing five or six weeks after operation despite an apparently aseptic technic of removal. Eugene Bernstein, working with Beer, was able to demonstrate the suspected traumatic bacillemia in three of thirty controlled cases using inoculation of systemic venous blood into guinea pigs before and after operation. In 1929 Beer pointed out that in the cases of nephro-ureterectomy there was marked difference in the healing of the two wounds created by the surgeon. The anterior pararectus incision employed to expose and divide the ureter as near the bladder as possible healed regularly by first intention, despite the proximity of the diseased ureter stump in its depths. The lumbar wound, on the other hand, presented an identical incidence of tuberculous wound infection as in the series of simple lumbar nephrectomies. The explanation for this phenomenon appeared to him to be that the ureteral wound was made through the avascular rectus fascia, the rectus muscle being retracted, not incised, whereas the lumbar wounds in both groups of cases was made through the vascular muscles of the lateral abdominal parietes. In a more recent report made by Beer and Edelman three cases of thirty-eight "aseptic" nephro-ureterectomies developed mild infection of the anterior rectus sheath incision. In one, an abscess formed about the ureter stump twenty-six days after operation—the wound having healed before this abscess developed. In the second, there was gross spilling of pus on cutting through the pelvic ureter between the ligatures. In the third, the pelvic ureter was very adherent and was considerably traumatized during its isolation. The conclusion that bacillemia is responsible for the lumbar wound infections and not local contamination seems questionable in view of the explanation given for these three anterior ureteral wound complications. That traumatic operative tubercle bacillemia explains the occasional development of subacute miliary tuberculosis, tuberculous meningitis, or even early involvement of the remaining kidney

(Israel) seems reasonable. That it is responsible for wound tuberculosis forces one to fall back upon the theory of locus minoris resistentiae.

The advisability of instituting drainage of the renal fossa, closing the rest of the wound by suture has received but scant attention.

W. J. Mayo in 1912 advocated closure of the wound without drainage when no gross soiling occurred. If there was any soiling he filled the wound with normal saline during closure in the belief that the rapid absorption of the fluid would carry away the diluted infectious material.

Hunt, in 1923, advised against drainage and stated that complete closure gave a high percentage of primary unions.

Most operators drain because they fear oozing and exudation of serum into the renal fossa. The old axiom of omitting drainage in the surgery of tuberculous lesions has been almost completely disregarded in dealing with the tuberculous kidney.

THE TECHNIC

Convinced that the solution of the problem was dependent upon meticulous avoidance of direct infection of the wound during removal of the diseased kidney and ureter, and upon complete closure of the wound without drainage, I adopted the following technic in 1929. It was desirable, too, that dissemination of bacilli into the circulation should be minimized to avoid secondary deposits, just as in dealing with renal malignancy.

Anesthesia. Spinal analgesia is employed whenever possible. Pontocaine, 20 mgm., or procaine 150 mgm. is injected with four or five cubic centimeters of spinal fluid between the first and second lumbar vertebrae. The patient is kept flat on his back for at least five minutes before being placed in the usual kidney position. This permits of observing the patient's reaction and of starting intravenous infusion of five per cent glucose in saline if there is an unusual fall in blood pressure. The grave reactions are more frequent when patients are immediately placed on the kidney bridge and the table broken before the analgesic agent has had an opportunity to become fixed near the level of the injection.

The excellent relaxation obtained makes for ease of exposure and gentleness in handling the tissues. The relatively little bleeding from the wound surfaces minimizes the amount of catgut necessary to obtain perfect hemostasis, and so, too, the amount of tissue devitalized by ligatures.

When spinal analgesia seems inadvisable, as in children, avertin supplemented by gas-oxygen or ether is employed.

Incision. The usual oblique lumbar incision is employed but it is extended well forward and downward beyond the level of the anterior superior spine of the ilium. This permits easy exposure of the ureter below the lower limits of the pararenal (Gerota's) fascia. Laparotomy pads are clipped to the edges of the wound.

The ureter is freed with its surrounding connective tissue sheath from the peritoneum anteriorly and the parietes posteriorly. This sheath must not be opened; the ureter must not be stripped out of it. By blunt and sharp dissection the ureter with its surrounding sheath is freed as far down as possible, usually to or below the point where it crosses the iliac vessels.

A chromic catgut ligature is then placed and tied securely around the ureter and its sheath at the lowest level and a second ligature similarly about 1.5 cm. higher up. Packing is carefully placed beneath and around the ureter to protect the surrounding tissues. Laparotomy pads protect the peritoneum anteriorly and the parietes posteriorly. The ureter is partly divided with a phenolized scalpel between the two ligatures; the lumen is thoroughly carbolized on both sides with a small hemostat dipped in the pure phenol. Severance is completed and the knife discarded. The lower ligature is cut and the distal stump dropped. The proximal stump is covered with a small pledget of gauze and this in turn by a piece of rubber dam fastened over it by a heavy silk ligature. The free end, thus protected, is now delivered out of the wound. The pads, packings, and retractors are removed and discarded. The operator and first assistant put on fresh gloves.

The freeing of the kidney is then begun by working *outside* of the pararenal fascia. The object is to leave the perirenal fat as a protective cushion against squeezing of the kidney, minimizing the traumatic entry of bacilli into the renal vein. Posteriorly the pararenal fascia is readily separated from the muscular parietes (quadratus, psoas). Anteriorly the cleavage plane between it and the peritoneum is readily found and the latter pushed forward and retracted under a protecting pad.

The ureter is now followed upward anteriorly and here Gerota's fascia must be incised to expose the vascular pedicle. Extending the incision a little further upward, the suprarenal gland will come into view. The mesial inferior tip of this structure is in close proximity to the renal pedicle, particularly on the left side of the body. This gland is now carefully freed from the kidney and its vessels clamped and carefully ligated. It is now possible to deliver the kidney encased in its perirenal fat and pararenal fascia, except where the vascular pedicle is attached.

The vascular pedicle is carefully cleared as far away from the kidney as feasible. Using a Deschamps, a strong chromic catgut ligature is passed between the artery and vein and tied—first around the one, then about both structures. A second ligature is similarly placed and tied a few millimeters nearer the kidney and then a Carmalt clamp is applied still nearer the kidney. A carbolized knife cuts the pedicle between the clamp and the second ligature and the specimen is removed.

It is of utmost importance that no blood be allowed to escape into the wound from the proximal (renal) end of the renal vein because such blood may contain bacilli liberated during the manipulations described.

The wound will be found clean and dry with no loose fat. The table is unbroken, the bridge dropped and the usual simple closure of the abdominal muscles performed with figure of 8 chromic catgut including the lumbar fascia and all the muscles. These should not be tied too tightly for fear of causing necrosis. The skin may be closed with silk or by Michel clips, the latter being preferable.

If subtotal ureterectomy is indicated the first step of the procedure is the exposure of the lower ureter through a pararectus incision (Kammerer) while the patient is in the supine position. The rectus muscle is retracted mesially, the peritoneum separated from the parietes, and the ureter exposed extraperitoneally where it crosses the iliac vessels. The ureter with its sheath intact is separated from the peritoneum and freed as far downward and upward as the limits of the incision permit. The division of the ureter with its sheath is carried out as near the bladder as possible, observing the same precautions as in the technic described for lumbar nephrectomy. The proximal ligated free end of the ureter—covered by gauze and rubber dam as previously outlined—is dropped back into the depth of the wound. The latter, hemostasis being meticulously attended to, is closed in layers without drainage.

The patient is now placed in the usual kidney position, the lumbar incision is made and the freeing and delivery of the rest of the ureter easily accomplished. The kidney is then removed exactly as in the lumbar nephrectomy described. The operation is termed aseptic ureteronephrectomy and seems preferable to nephro-ureterectomy for tuberculosis and for tumors involving the ureter and renal pelvis. Its chief advantages are that the patient's position on the table has to be changed only once during the operation, and that the opportunities for extraneous infection are materially diminished. The argument that it is better to explore the kidney first does not apply because the pathology and indications have usually been determined by the urologic investigation.

RESULTS

A brief abstract of the pertinent data in the cases operated upon by me according to this technic is herewith appended.

Case 1. 1929; Beth-El Hospital Adm. 36631. R. D.; male; age 21. Backache, hematuria, pyuria five weeks. Lesion of right kidney— ulceration of pelvis, upper and middle calyces; calcific foci in parenchyma; thickened ureter. Right nephrectomy October 11, 1929. Discharged October 25, 1929. Complete and lasting primary union.

Case 2. 1930; Hospital for Joint Diseases Adm. 28488. M. S.; male; age 52. Pulmonary TBC 1912. Right renal colic 1915. Hematuria in 1927. Right epididymectomy for tuberculosis in 1929. Present lesions— tuberculosis of prostate and right seminal vesicle. Right renal tuberculosis and vesical tuberculosis. Lesion of right kidney—ulcerated and calcific lesion of upper pole calyces; cortical subcapsular tubercles;

greatly thickened ureter. Right nephrectomy July 3, 1930. Complete and lasting primary union. Left orchidectomy for tuberculosis in 1934. Urine negative July 19, 1935.

Case 3. 1930; Beth-El Hospital Adm. 44523. F. S.; female; age 22. Hematuria, pyuria, dysuria three months. Pregnant seven weeks. Lesion of right kidney—calycitis of lower pole with calcification, stenosis and large abscess of lower pole; tuberculous ureteritis. Right nephrectomy December 23, 1930. Dilatation of cervix and curettage January 2, 1931. Discharged January 8, 1931. Complete and lasting primary union.

Case 4. 1932; The Mount Sinai Hospital Adm. 336750. A. K.; female; age 41. First examined by me in February, 1931 for frequency, hematuria, tenesmus of one year's duration. Extensive severe vesical tuberculosis, tuberculosis of left kidney established; right ureter could not be catheterized; intravenous urography not conclusive. Patient sent to Florida for general hygienic treatment with excellent general improvement and amelioration of bladder symptoms. November 2, 1931 right ureter was catheterized; good function; rare leucocyte; no tubercle bacilli found. Two guinea pigs inoculated, one showed a few tubereles in the spleen only. Lesion of left kidney—diffuse ulcerous and caseous calycitis, pyelitis and ureteritis. Left uretero-nephrectomy January 14, 1932. Rapid pulse, anemia and weakness relieved by transfusion. Complete and lasting primary union of both anterior and lumbar wounds. Discharged February 14, 1932. Developed drowsiness, diplopia March 24, 1932. Readmitted to hospital. Lumbar puncture yielded clear fluid under pressure; sugar content greatly reduced; 150 lymphocytes per c. c.; no tubercle bacilli found; guinea pig inoculation negative. X-ray examination of chest showed marked infiltration of right upper lobe and calcific lesions at apex of lower lobe. Patient developed stiff neck, left external rectus palsy, left facial weakness, convulsions beginning with the left arm, then coma and rapidly mounting temperature. Ceased March 31, 1932. Diagnosis—tuberculous meningitis although spinal fluid was negative. No autopsy. Status of the remaining kidney not determined.

Case 5. 1932; The Mount Sinai Hospital Adm. 338308. G. R.; male; age 41. Left epididymectomy for tuberculosis sixteen years ago. Few weeks later similar lesion developed on right side requiring same procedure. For past four months frequency, burning and pyuria. Lesion of right kidney—calcific lesion of upper pole with ulceration of upper calyces. Localized lesion; rest of kidney and ureter normal. Right nephrectomy May 6, 1932—the perirenal fat was densely adherent at the upper pole and had to be cut through to free the kidney (office record). On May 18, sutures removed, apparent primary union. Next day profuse serous discharge from middle of wound. Discharged from hospital May 28, 1932 with several sinuses in the scar. The main sinus led into the renal fossa. The wound was finally healed September 6, 1932 after natural heliotherapy, sun baths general and to the wound.

Case 6. 1933; Hospital for Joint Diseases Adm. 43085. E. H.; female; age 23. Marked lumbodorsal scoliosis since age of 10, not tuberculous; convexity to left in lumbar area. Left renal colic six months ago; pus and blood found in urine. Brief period of frequency and tenesmus four months ago. No subjective symptoms now. Lesion of left kidney—calcification in lower pole, caseous calycitis with subcapsular cortical involvement and marked perinephritis. Upper ureter involved. Left nephrectomy May 29, 1933 under ethylene, oxygen, carbon dioxide anesthesia. Kidney very high up, exposure difficult because of scoliosis. Lower pole perinephritis involved Gerota's fascia with adhesion to the peritoneum. Discharged June 19, 1933 with primary union. On July 25 there appeared a slight serous discharge from posterior third of the scar which healed in a week.

Case 7. 1935; Jewish Hospital Adm. 184058. S. B.; male; age 24. Dull pain in left flank; pyuria, dysuria three weeks. Tuberculous ulceration about left ureteral orifice. Lesion of left kidney—tuberculous papillitis and calycitis in upper pole—very recent lesion. Left nephrectomy August 23, 1935. Discharged September 4, 1935. Complete and lasting primary union. Negative urine August 27, 1936.

Case 8. 1935; Hospital for Joint Diseases Adm. 55905. T. S.; female; age 50. Treated in 1922 for stone in kidney (?). Weakness of back in 1931, then kyphosis at level of D 10. Spine fusion November 9, 1932 for Pott's disease. In October 1935, frequency, urgency, and burning. Vesical and left renal tuberculosis. Lesion of left kidney—cavernous pyelitis and calycitis with sacculations; ureter 1.5 cm. in diameter palpable by vagina. Left nephrectomy November 18, 1935. Six days later sudden sharp pain in wound but nothing abnormal found. Discharged December 4, 1935. Wound completely healed. December 17, 1935—stitch abscess noted in Out-Patient Department; then developed typical tuberculous sinuses, pus from which gave positive guinea pig test. Wound revised August 24, 1936. Wound healed solidly June 18, 1937.

Case 9. 1935; Jewish Hospital Adm. 186176. G. P.; female; age 34. Right lumbar pain, frequency, dysuria, hematuria six weeks. Acute ulcerous cystitis right half of bladder. Lesion of right kidney—diffuse tuberculous calycitis, pyelitis and ureteritis, many parenchymatous lesions up to one cm. diameter. Right nephrectomy December 9, 1935. Complete and lasting primary union. Urine negative May 2, 1936. Developed lupus lesion near left inner canthus October 3, 1936. Now well.

Case 10. 1935; Jewish Hospital Adm. 186398. B. L.; male; age 53. Rejected by insurance examiner ten months ago because of pyuria. Frequency and severe dysuria two months. Lesion of left kidney—upper pole studded with subcapsular tubercles; cavity 3 by 1.5 cm. in upper pole; pelvis and ureter studded with tubercles. Left nephrectomy December 16, 1935. Subcutaneous emphysema of scrotum, penis, and

groins after operation disappeared spontaneously. Complete and lasting primary union. Urine negative October 25, 1936.

Case 11. 1936; Jewish Hospital Adm. 187771. S. F.; male; age 58. Left orchidectomy for tuberculosis two years ago. Right epididymectomy for tuberculosis one and one-half years ago followed by abscess of scrotum. Prostate and vesicles involved. Frequency and dysuria four months. Lesion of left kidney—tuberculous calycitis, pyelitis and ureteritis. Left nephrectomy February 2, 1936. Complete and lasting primary union.

Case 12. 1936; Hospital for Joint Diseases Adm. 58192. W. F.; male; age 5. Pulmonary tuberculosis at age 2. Present lesions—bilateral tuberculous otitis media, tuberculous sinus of lymph nodes in right parotid gland. Hematuria, pyuria, dysuria one year. Lesion left kidney—tuberculous pyonephrosis (16 by 9 by 4 cm.), pyelitis and ureteritis. Left nephrectomy April 22, 1936. On May 16, 1936 there was a slight serous discharge which ceased in a few days. Complete and lasting healing thereafter.

Case 13. 1936; Hospital for Joint Diseases Adm. 58185. N. G.; male; age 24. Frequency, nocturia one year. Hematuria and urethral discharge few months. Granulomatous lesion near right golf hole ureter. Calcified lesion upper lobe right lung. Calcific deposits in liver and spleen. Lesion of right kidney—tuberculous pyonephrosis (12 by 7 by 4 cm.) and ureteritis; lymphadenitis retroperitoneal. Right nephrectomy April 24, 1936—removed tuberculous lymph node. Complete and lasting primary union.

Case 14. 1936; Jewish Hospital Adm. 192371. I. B.; male; age 43. In 1934 right orchidectomy for tuberculosis. Chest X-ray examination showed healed calcified lesions. Urine contained tubercle bacilli then. Frequency, dysuria three months. Lesion of right kidney—pelvis and calyces distended with pus, scattered tubercles in parenchyma, periureteritis. Right nephrectomy June 24, 1936. Complete and lasting primary union. Left renal colic and passage of small calculus October 1, 1936.

Case 15. 1936; Jewish Hospital Adm. 192780. M. K.; male; age 44. Right renal colic and passage of stone eighteen years ago. Left loin pain, frequency and dysuria six months. Lesion of left kidney—calycitis with calcification; ureteritis. Left nephrectomy July 9, 1936. Complete and lasting primary union. Discharged July 20, 1936. Activation of pulmonary lesion with dry pleuritis August 13, 1936. This subsided. Patient known to be well October 28, 1937.

Case 16. 1937; Hospital for Joint Diseases Adm. 66546. T. W.; female; age 9. Previous spine fusion for lumbar Pott's disease; previous fusion operation for right tuberculous coxitis. Pyuria, hematuria four months. Lesion of left kidney—tuberculous pyonephrosis, massive, with B. coli secondary infection. Left nephrectomy October 18, 1937. Com-

plete and lasting primary union. Discharged October 31, 1937. Healed at time of this report.

SUMMARY AND CONCLUSIONS

In sixteen cases of renal tuberculosis, one of which may have been bilateral, uretero-nephrectomy was performed in one case; nephrectomy and partial ureterectomy without drainage, according to the technic described, in fifteen cases. The lesions varied from the early type to the most advanced. The patients were children, young adults, and older adults. Known tuberculous lesions had been present in other parts in eight cases. One patient whose renal lesion may have been bilateral (case 4) upon whom uretero-nephrectomy was performed with primary union of both wounds, died of tuberculous meningitis ten weeks after operation.

In twelve cases complete and lasting primary union of the wound was obtained. In two cases (Cases 6 and 12) an ordinary serous discharge of brief duration occurred during convalescence but gave no clinical evidence of infection. In two cases (Cases 5 and 8) tuberculous wound infection occurred. In case 5 densely infiltrated fat adherent to the upper pole lesion was cut through and some of this tissue left in situ. In case 8 a satisfactory explanation of the failure is not apparent.

Although this series of sixteen cases is small, the wide variety of renal lesions and the wide age range of the patients leads me to believe that nephrectomy without drainage for tuberculosis, carried out by the technic described, will yield primary union and no evidence of wound tuberculosis in 85 to 90 per cent of cases. I am convinced that the problem is one of avoiding local contamination of the renal fossa and the wound surfaces, and the omission of any kind of drainage.

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OBSTRUCTIVE UROPATHIES IN CHILDREN

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Within recent years the subject of urinary tract obstruction in children has become one of increasing concern to the urologist and pediatrist. An inevitable outcome of this interest and coöperation between the specialties has been a rising number of contributions to the literature on all phases of the problem. Whereas reports of a decade or two ago abounded in post mortem studies of obstructive urinary tract lesions and their inevitable sequelae, to-day we find clinicians occupied with preventive measures— earlier diagnosis and improved methods of therapy.

Two outstanding milestones in urologic history are noteworthy in the evolution of pediatric urology: the introduction of miniature cystoscopes and instruments patterned after the adult armamentarium, and intravenous urography. Nitze, in the 1907 edition of his cystoscopic handbook, stated that while a 5 mm. cystoscope could be used in certain instances in eight year old boys, the narrowness of the urethra in those under ten years of age generally prevented the use of the instrument.

In 1911, Beer (1) reported the perfection and successful application of a miniature cystoscope, after a trial period of four years. It represented a real contribution, inasmuch as the existing Nitze and Portner models were inadequate, due either to excessive calibre, length or flexibility. An interesting commentary on the development of cystoscopy in children is gleaned from Dr. Beer's concluding paragraph in his contribution of 1911: "The youngest patient cystoscoped by me was a little girl of fourteen months and the picture of traumatic ulcers and cystitis following the use of a stone searcher were readily seen. The youngest male child that I have cystoscoped was five years old. The youngest patient whose ureters I have catheterized was a girl of five years. This was done without anesthesia. The youngest boy was ten years old."

To-day, thanks to the ingenuity and combined efforts of instrument maker and urologic instrumenteur, cystoscopic examinations have been reported in the first week of life. Our youngest subject was a three months' old boy in whom retrograde pyelography was done. The resultant X-ray (Figs. 1 and 2) not only depicts the result of our efforts, but demonstrates a lesion germane to the subject of this paper.

With the advent of intravenous urography in 1929, a valuable procedure was added to diagnostic urology. As we have already shown, the introduction and perfection of miniature cystoscopic instruments, figuratively

as well as literally brought light to the abyss that was pediatric urology. This overcame the timidity of the urologist in instrumenting children. Next came the problem of convincing the parent, as well as the family physician, that such a procedure was indicated.   Intravenous urography, purely as a diagnostic *aid*, has supplied perhaps the most convincing argument, where pathology is disclosed, for further indicated instrumentation or surgery.

We have digressed to give a brief insight into the historical development of pediatric urology because it also forms the background for a study of obstructive uropathies in children.   Let us consider a single obstructive lesion and trace its history.   Valvular obstruction of the posterior urethra was first described at autopsy by Langenbeck in 1802.   It was noted in life, as an accidental finding, by Eigenbrodt, in 1891.   Not until 1913 was it recognized in a living boy, when Hugh Young diagnosed the lesion through a cystoscope.

Young, Frontz and Baldwin (2) in 1919 reported a series of valvular obstructions and six years later Hinman and Kutzman (3) presented six personal cases together with fifty collected from the literature.   Whereas all of the latter cases were diagnosed during life by cystoscopy, thirty-two, or 64 per cent, of the previously recorded ones were *post mortem* findings. Prior to 1919, twenty-four of the fifty collected cases were found at necropsy and only three in life.   Since 1919, however, eight were found post mortem and eighteen in life.   Such historical data represent a record of commendable past performance and one of future promise for earlier diagnosis, more efficacious therapy, and the introduction of preventive measures in combating obstructive uropathies in particular, and pediatric urologic lesions in general.

GENERAL CONSIDERATIONS

The high incidence of congenital anomalies in children predisposes to the menace of partial or complete interference with the normal flow of urine.   As opposed to a 2.3 per cent incidence of urinary tract anomalies in 4, 903 autopsy reports reviewed by Bugbee and Wollstein (4), Bigler (5) noted a much higher occurrence, 13 per cent in a series of 153 consecutive necropsies in children.   Clinically, Hyman (6) found congenital anomalies to be the underlying factor in an analysis of 150 instances of urologic maladies in children.

Stasis and either potential or actual back-pressure changes accrue from obstruction, whatever its cause.   With the interruption in the continuity of urinary flow, one must contend with the ever-present hazard of infection, and the triad of obstruction, stasis and infection presents one of the most serious hazards with which its victim and the physician have to cope.   Obstruction usually antedates infection but the sequence may be reversed.   In such instances as recurrent pyelonephritis, tuberculosis, or

gonorrhea, local tissue reaction with its attendant edema, scarring or stricture formation may so impair the urinary channel as to partially or completely interfere with the passage of urine.

The degree and location of obstruction play an important rôle in the extent of tissue destruction before subjective or objective signs manifest

FIG. 1. X-ray picture, taken ten minutes after pyelogram, showing residuum of contrast medium in pelvis and ureter with uretero-vesical (intra-mural) constriction. This child of three months had a congenital absence of the left kidney and ureter and stenosis of the anus and rectum for which colostomy was performed shortly after birth. The shadows lying to the inner aspect of the lower ureter represent barium in the distal segment of the colostomy given to determine the extent of its patency.

themselves. Broadly speaking, we classify an obstruction as infra-vesical or supra-vesical. The infra-vesical lesion may present itself at any point from the external urinary meatus to the internal sphincter. Because

such pathology manifests itself usually by impaired micturition it is symptomatically more evident and therefore not often therapeutically neglected.

Supra-vesical obstruction, confined to the ureterorenal segment, is accompanied by fewer signs and symptoms of dysfunction. Since the point of obstruction is closer to the kidney and since that structure represents the most essential organ of the urinary tract, the severity of such lesions
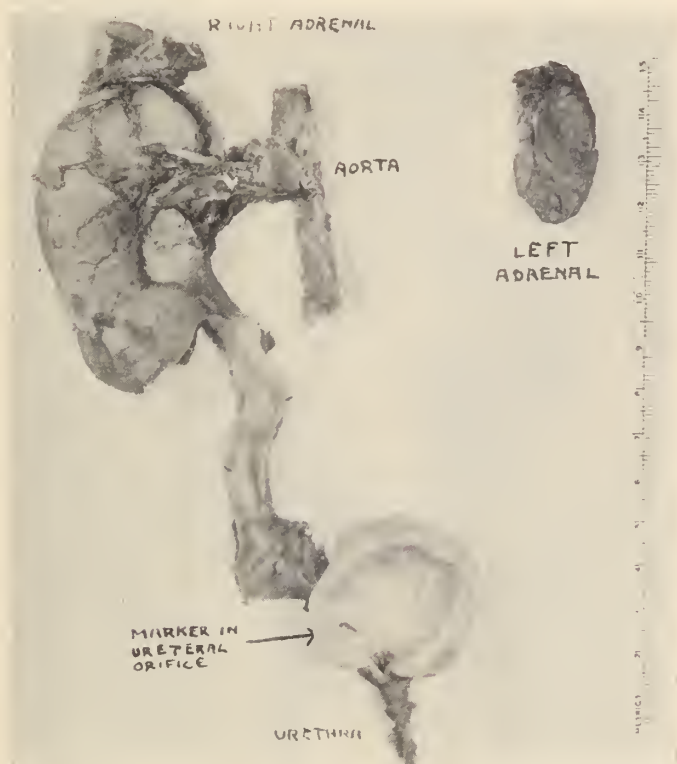
FIG. 2. Pathological specimen demonstrating degree of ureterectasis and pyelectasis. It was difficult to introduce even a filiform through the solitary ureteral orifice. Despite the absence of the left kidney, a normal left adrenal was found.

can be appreciated. Most often they are unilateral, although recent interest has led to greater appreciation of bilateral neurogenic lesions. Differentiation between dynamic mechanical and adynamic neurogenic obstruction is difficult, although the ultimate changes are the same. In the ensuing paragraphs we shall consider etiological factors, the pathological changes wrought by them and the diagnostic and therapeutic approach to the clinical problem.

Urinary tract obstruction usually finds its origin in congenital anomalies and, less often, from acquired lesions. At times, superimposed infection or tumefaction becomes the final insult to a harmlessly existing anomaly. Disturbances secondary to involvement of the central or peripheral nerv-

Fig. 3. Urogram of entire urinary tract in a newborn with atresia of the bulbous urethra. Sodium iodide was injected through the anterior bladder wall to permit urographic delineation. Fortunately, the specimen was removed without disrupting the urethral occlusion. Note marked dilatation of posterior urethra, urachal pouch and upper urinary tract.

ous system represent a group which is slowly being classified and the *modus operandi* clarified.

In the *urethra*, congenital lesions include atresia, stricture, diverticulum, posterior urethral valves, and hypertrophy of the verumontanum. Acquired conditions are stricture, urethrocele, calculus, neoplasm and diverticulum. Phimosis and paraphimosis, either congenital or acquired, may contribute indirectly to even severe urethral obstruction.

Complete atresia of the urethra must, by its very nature and location, eventuate in death if the obstruction is unrelieved. The accompanying urogram and specimen (Figs. 3 and 4) bear mute evidence of such a condition in a child who lived one hour. The complete case report and consideration of the condition has been presented elsewhere by Woodruff and Milbert (7). The marked dilatation of the posterior urethra, bladder, ureters, and the conversion of both kidneys into cystic masses attest to
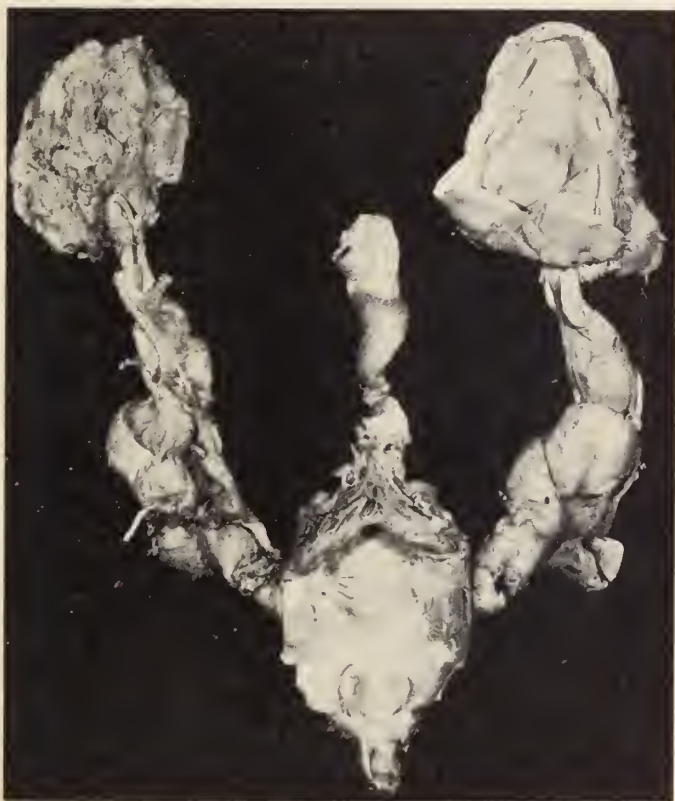
Fig. 4. Autopsy specimen of same case, showing extent of tissue destruction from back-pressure. Note stretching of internal sphincter, pouch-like posterior urethra, and conversion of kidneys into cystic sacs. (From case report by Woodruff and Milbert (7).)

the effect of hydrostatic pressure over a period of four months, assuming that urinary secretion begins in the fifth month of gestation.

As opposed to the extreme degree of obstructive uropathy above depicted, there is one of chronicity in a boy of 15, with posterior urethral valves. His urogram (Fig. 5) shows the extent of damage when partial obstruction persists over a period of years. The exposure was made following introduction of a catheter into his bladder and instillation of the

contrast medium.   Insufficiency of control of the ureteral orifices resulted in reflux up both ureters.

FIG. 5. Retrograde urogram showing marked obstructive phenomena in boy with posterior urethral valves.   Note funnel-shaped urethro-vesical shadow.   (Courtesy Dr. S. R. Woodruff.)

We have seen several instances of urinary obstruction in children due to hypertrophy of the verumontanum.   Bugbee and Wollstein (8) stimulated interest in the subject by their report on eight cases from the Babies

Hospital. Since that time at least a score of case reports have found their way into the literature.

Vesical disturbances resulting in obstruction include contracture of the neck, cysts and diverticula, among congenital lesions, while acquired pathology, in addition to the above mentioned, is due to calculus, neoplasm or vesical and sphincteric dysfunction, due to peripheral or central nervous system derangement. Contracture of the vesical neck has been

Fig. 6. Advanced hydronephrosis due to uretero-pelvic constriction by aberrant vessel. Nephrectomy was performed on this boy, aged 8. (Courtesy Dr. S. R. Woodruff.)

emphasized as an infrequent, yet often overlooked, cause of obstruction in children by Edwin Beer (9, 10) his first contribution on the subject having been made in 1915 and another in 1924. The etiology of this lesion with its accompanying hyperplastic mucosal changes or actual fibrosis is a debatable subject, since some of the cases are obviously congenital in origin, others represent acquired infective processes, and finally a small group appear to be neurogenic, yet without conclusive demonstrable nerve pathology.

Ureteral conditions predisposing to obstruction are congenital valves, folds, strictures, ureterocele and constriction by aberrant vessels. Calculus, neoplasm, stricture, angulation or infection represent acquired processes. Of renal origin one may cite anomalies of the pelvis, aberrant renal vessels crossing and constricting the pelvic outlet, and abnormal positions of the kidney. Calculus, neoplasm or nephroptosis are acquired conditions.

By far the most common cause of the uretero-pelvic obstructive syndrome is constriction by aberrant vessels. The site of greatest predilection lies at the uretero-pelvic junction and often asymptomatic progress of the lesion makes it a particularly serious one (Fig. 6). Constriction by the uterine artery or by the vas deferens in the lower ureteral segment has been reported, but represents a rarity. In effect, the etiology of such uropathies is extra-urinary.

Other *extra-urinary* factors play a rôle in the production of obstruction. Adynamic stasis resulting from neurogenic pathology has been cited. It manifests itself in disturbed innervation to the bladder and its sphincter and less often to atonicity of one or both ureters. Pelvic masses representing either anomaly, infection or new growth, may impinge upon one or both ureters or the urethra. Campbell (11) details instances of urinary obstruction produced by sacral teratoma, enlargement of the vagina and uterus secondary to vaginal atresia, similar enlargement of the rectum behind an anal stricture, hematoma of the psoas muscle constricting the overlying ureter, an enlarged leukemic retroperitoneal lymph node causing ureteral obstruction and plugging of both ureters by blood clots in a case of hemorrhagic disease of the newborn. Two instances of massive hematocolpos behind an imperforate hymen have come to our attention. These resulted in partial and complete urethral obstruction, causing in one instance "paradoxical" incontinence and in another acute retention of urine.

PATHOLOGY

The effect of prolonged, unrelieved urinary obstruction is dependent on principles of hydrodynamics. The urinary apparatus is a tubular channel, as represented in the ureters and urethra, with conveniently interposed "buffers"—the renal pelves and the bladder. Despite Nature's provisions, the hydrostatic pressure created by continued secretion of urine behind a complete or partial obstruction cannot be long denied without extensive tissue destruction due to pressure atrophy and circulatory impairment with resultant tissue anemia.

An obstruction at any point in the normally continuous path from glomerulus to external meatus will inevitably result in changes above that site. Uretero-pelvic juncture obstruction involves the pelvis and renal substance, while a lesion of the urethra will, in turn, affect urethra, bladder, ureter and kidneys, if unchecked.

Irrespective of its cause, obstruction produces characteristic changes in the affected segments of the urinary tract. Urethral obstruction is characterized by dilatation and infection, or, congenital defect may so weaken the urethral wall as to cause diverticulum formation, or even extravasation. Vesical changes include hypertrophy, trabeculation, cellule formation, diverticulum and ultimately complete dilatation, due to the attempt of the viscus to empty its contents against a barrier. Similarly, the detrusor musculature and inter-ureteric ridge become hypertrophied.

The ureter, whether directly or indirectly involved, may show hypertrophy or dilatation, with elongation, angulation and loop formation with adhesive bands stretching across the segments. The renal pelvis may show an initial hypertrophy but soon dilates under the stress of continuous unrelieved intra-luminary pressure. An extra-renal pelvis acts as a better buffer in contradiction to the intra-renal type with its earlier and more extensive kidney involvement. Conversion of the pelvis and kidney into a cystic mass of varying size—massive obstructive hydronephrosis—represents the end result. The final stage, with infection sooner or later supervening, is typified in infected hydronephrosis or pyonephrosis.

Hinman (12) and his associates have, by extensive animal experimentation, contributed greatly to the subject of hydronephrosis, its mechanism and sequelae. The progressive dilatation, collapse and eventual atrophy of the excretory unit has been well shown by them. With this crippling or actual destruction of the fundamental unit of the kidney, retention of nitrogenous waste products in the blood stream is inevitable. The clinical picture of uremia is frequently most prominent in cases with infra-vesical obstruction, where both kidneys are involved. From his studies on hydronephrosis, Hinman (13) evolved his theory of renal counterbalance which has as its basis the compensatory hypertrophy of one kidney when its hydronephrotic mate suffers impaired or complete loss of function.

SYMPTOMATOLOGY

Clinical signs and symptoms of urinary obstruction depend upon the site of the lesion and the presence or absence of infection. An infra-vesical obstruction is characterized by alterations in the act of micturition, while supra-vesical types, especially when unilateral, may be relatively asymptomatic. In the absence of infection, the sole problem of interference with urinary flow is mechanical. Superimposition of infection is accompanied by an intensification of symptoms that already exist, plus those symptoms common to sepsis anywhere in the body.

Hydronephrosis or hydroureter may exist over a long period of time without symptoms. When the cystic mass assumes such proportion as to be visible to the eye as a result of body asymmetry, or palpable, or produce pressure by its very size and weight, we are confronted with the

final stage of pathology. Fortunately, routine physical examination and urinalysis may focus attention on the urinary tract. The passage of clots or kinking of the ureter may produce loin or abdominal pain with its characteristic radiation. Intermittent filling and evacuation of the hydronephrotic sac may be suspected when a history of variability in the size of an abdominal loin mass is reported.

We have been impressed with the frequency with which gastro-intestinal symptoms occur in the presence of upper urinary tract pathology. This is especially true of children and several instances come to mind of persistent medical and surgical treatment for pylorospasm, enteritis, appendicitis, colitis, or constipation, when the pathology lay in the urinary tract. Nausea, vomiting, obstipation, malnutrition, or intermittent abdominal colic feature such case studies. Later, and often too late, is a large hydronephrosis disclosed. We refer to this subject without malice to any particular group, but as a plea for earlier urologic investigation of children with gastro-intestinal symptoms in whom the etiology is vague.

Similarly, a persistent pyuria or cases classified as chronic pyelonephritis, where cause and effect are not easily correlated, should receive the benefit of early urologic study. A nephritic child with unusually high nitrogen retention in the blood may be the victim of unilateral or bilateral obstructive lesions. Any pyuria that persists after a fair trial of four weeks under medical supervision should have a complete urologic investigation.

The infra-vesical obstructive urinary tract lesions are marked chiefly by frequency, dysuria, hesitancy, urgency, impaired flow or terminal dribbling. A child with urethral or vesical neck obstruction may display all of the symptoms of the elderly victim of prostatic hypertrophy, since in each case a mechanical obstruction interferes with normal micturition.

Obstructions at or below the neck of the bladder, if untreated, eventuate in bilateral renal impairment. As a result of such destruction, retention of nitrogenous waste products in the blood leads to uremia. Occasionally the child is brought to the physician in such a state—the abdominal mass, pasty complexion, anemia, and weakness being tell-tale evidence of the underlying pathology.

Summarizing, therefore, tumor (hydronephrotic kidney, distended bladder), pain, pyuria, hematuria, difficulties in micturition or uremic manifestations are significant findings in obstructive uropathy. Infection, apart from its febrile toxic course, only intensifies preexisting symptoms. Calculi which form behind an obstruction may herald the first signs of pathology by the production of hematuria or colic.

DIAGNOSIS

A complete history, physical examination and urinalysis should form the basis for any evaluation of signs and symptoms. Upon this foundation the urologist builds his *complete* urologic study. We emphasize the

need for complete study because, with the exactitude of diagnostic agents at his disposal, the urologist should assume nothing. We have in mind a six year old child who had shown intermittent pyuria and had suffered from persistent gastro-intestinal upsets with associated malnutrition and maldevelopment for five years. An urologic study four years prior had been fruitless because the examiner deemed it unnecessary to study the left half of the upper urinary tract, during the course of cystoscopy and right uretero-pyelography. Uretero-nephrectomy for infected hydro-ureter and hydronephrosis (with functionless kidney) eventuated, followed by continuous general constitutional improvement. (Figs. 7 and 8.)

FIG. 7. Retrograde pyelogram showing hydro-ureter and hydronephrosis with superimposed infection in a girl of 6. Faulty osseous development of the vertebrae pointed to possible neurogenic etiology for the lesion.

Passage of urethral instruments—catheter, bougie or cystoscope—determines the patency of the urethra. Testing for residual urine after the child has emptied its bladder voluntarily may supply a clue to dynamic or adynamic obstruction. Cystometric studies of vesical wall tonicity may reveal a neurogenic basis for increased residual of urine.

Urographic studies may be especially informative, even before instrumentation is undertaken. *Intravenous urography* depends upon adequate kidney function and excretion. It may be used to advantage in all cases preliminary to cystoscopy and retrograde pyelography. In obstructive

lesions, the combined use of cystoscope and x-ray represent the ideal means of disclosing the etiology as well as the extent of pathology.

Cystoscopic examination of the posterior urethra may reveal an obstructing verumontanum, valves, constriction of the vesical neck, hyperplasia

Fig. 8. Surgical specimen of same case with marked dilatation of ureter and pelvis apparent. On section, a mere shell of renal tissue remained. Note how informative the pyelogram is, in delineating the nature and extent of pathology.

of tissue or sphincteric dysfunction from disturbed neurogenic innervation. The bladder wall may show definite evidence of work hypertrophy, in the form of trabeculation, in overcoming an infravesical obstruction. Inspection of the ureteral orifices is afforded and any intrinsic or extrinsic cause for obstruction may be noted. *Cystography* may be used to corroborate abnormal urethral or vesical pathological findings.

Ureteral catheterization and *uretero-pyelography* are invaluable in localization and determination of the exact cause of obstruction, especially uretero-pelvic constrictions. In addition, by the use of suitable dyes, such as indigo carmine or phenolsulphonphthalein, fairly accurate determination of the function of each kidney can be made. Knowledge of this functional capacity is most important in determining one's therapeutic course and in rendering an opinion on prognosis.

TREATMENT

Relief of retention is the prime prerequisite to successful therapy. In addition to this conservation of function, one must aim toward preservation of tissue and corrective repair of the obstructive lesion. Naturally such a plan of attack is dependent upon accurate diagnosis and physiologic capacity of the body as a whole, and the organ or organs involved.

In lower tract obstruction preliminary drainage may be instituted by catheter per urethram or by cystostomy. The danger of rapid decompression cannot be too strongly emphasized. Hemorrhagic cystitis, nephritis, edema and even complete anuria may occur. In conjunction with gradual decompression it is essential to combat body dehydration and promote excretion of retained nitrogenous waste products. Fluids should be forced by all routes as needed—orally, hypodermatically or intravenously. Saline and dextrose make a satisfactory solution for either hypodermoclysis or intravenous infusion. Blood transfusions are exceedingly helpful, especially in victims of long-standing obstruction where anemia is one of the prominent signs of the uremic state. In acidosis in children we have had favorable experience with Hartman's lactate solution administered intravenously.

Unilateral obstructions of the upper ureter and kidney, in the presence of an adequately functioning kidney on the opposite side, may not only be relieved, but correction of the impediment should be undertaken at the same time. Under all circumstances conservation of renal tissue in the child is imperative. A cystic organ that may appear hopelessly inadequate may show remarkable return to function, once the obstruction is relieved. Likewise, when bilateral obstructive lesions are present, nephrostomy, either unilateral or bilateral, should be done early. At a later date and with appreciable return of renal function, further corrective plastic surgery or secondary nephrectomy may be undertaken. Open surgery is usually necessary in upper urinary tract obstructions, whereas in urethral and bladder neck obstructions the pathology may often be removed transurethrally through the operative cystoscope and by the use of physical agents.

PROGNOSIS

The future of a child with an obstructive uropathy depends upon the extent of the obstruction and the degree of functional impairment. Un-

fortunately, since congenital anomalies represent such a common offender and since in many instances the obstruction operates from birth, the patient as well as the attending physician are placed at a distinct disadvantage. Bilateral obstructive uropathy or a unilateral lesion in a solitary kidney must carry with it a poor prognosis. Furthermore, such children are either in the pre-uremic or uremic state and the body resistance is low. Intercurrent infections are common and often prove to be the deciding factor in producing a fatal outcome.

Years may be added to the life span of even badly afflicted children by a judicious choice of procedure. Proper decompression, respect for the principles of renal counterbalance, maintenance of body resistance and nourishment are essential. The ever-increasing number of *clinical* case reports and therapeutic successes, as opposed to *post mortem* findings, which characterized the literature on obstructive uropathy in children a decade or two ago, sounds a very hopeful and encouraging note. However, neither the continued interest nor the combined efforts of pediatrist and urologist can be abated if one heeds the statement of Campbell (11) that various combinations of obstruction and infection constitute over 90 per cent of the major urologic problems in children.

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ROENTGEN THERAPY OF KIDNEY TUMORS

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Evidence is slowly accumulating of the effect of external irradiation by deep Roentgen ray therapy on kidney tumors, both in Wilms' tumors of children and the tumors of adults. This evidence has two sources. First, the pathological changes observed in removed kidney tumors which, previous to removal, have been irradiated. Second, the clinical evidence of regression in tumors under X-ray therapy.

We have for some time stressed the opinion that under X-ray therapy the regression of Wilms' tumors should be as permanent as the regression obtained in the embryonal type of teratoid tumors of the testicle. Up to a few years ago, we were able to obtain under the same dosage of X-ray therapy used to control teratoid tumors of the testicle an extraordinary regression in the size of Wilms' tumors. Such regression, however, lacked permanency. Regression took place in several weeks. Then ensued a period of non-growth of the tumor, for perhaps several months. Subsequently the tumor grew again. The second regression under X-ray therapy was not as marked as the first and took a longer time. Finally the patient succumbed to the disease.

It was then believed, if the tumor-bearing kidney was removed after the first X-ray regression, that the operation was much less lethal and that cures would result. It is true that the operation was much more easily accomplished; but the cures showed no great increase. The patients usually succumbed from metastases. These metastases were either present at the time of the operation or the removal of the kidney set free metastasizing cells.

Such kidneys were subjected to a daily dosage of 300 R. at a distance of 50 cm. through three portals of entry until the patient received between 4000 and 5000 R. Sometimes the treatment had to be stopped short of this dose because of nausea or vomiting or because of a rapid drop in the white blood corpuscles. The former is probably a much more important reason for stopping the therapy than the latter. Certainly under this heavy daily dosage not much more than 4000 or 5000 R. could be given.

Then Dr. Ewing suggested that a much smaller daily dosage be given and continued over a much longer period—three or four months.

Case 1. The first patient was so treated by Dr. Walter McNeill (personal communication). The patient was a little girl, who was 14 months old when first seen by him September 13, 1934. A kidney tumor entirely filled her left abdomen. The pyelogram was typical. No pathological specimen was obtained. She was put on very low doses of high voltage X-ray—200 R. for two or three doses, then less than 100 R. daily for five months. The tumor entirely disappeared. She has had several courses of X-ray therapy since then. Now the child is entirely well three years and one month after first seen. She has gained eleven pounds and no tumor is palpable.

Case 2. H. S., Memorial Hospital No. 52472, a female, age 2 years, was admitted November 29, 1936. In December 1935 there had been noted difficulty in voiding and dysuria. The condition was diagnosed as pyelitis; no tumor was present at that time. In July 1936 the mother noticed a mass in the left abdomen. Her physician found a mass in the left upper quadrant of the abdomen extending almost to the umbilicus. The urine contained red and white blood cells and a trace of albumin. The blood count showed red blood cells 3,300,000; hemoglobin 60 per cent; white blood cells 6,400. Operation was advised but delayed. The patient continued to pass blood in her urine and the tumor increased in size.

On October 19, 1936 an intravenous pyelogram showed a tumor of the left kidney. She was given X-ray therapy—150 R.; 155 K. V. to the left kidney, anteriorly and posteriorly, every other day until she had received 450 R. to each portal. There was considerable regression of the tumor under this treatment.

The patient was now admitted to Memorial Hospital. Her physical examination showed in the left upper quadrant a mass extending 6 cm. below the costal margin, firm, somewhat movable on respiration and nontender. A pyelogram was typical of kidney tumor.

Deep X-ray therapy was started. To three portals of entry she was given 150 R. each day; 198 K. V.; 50 cm. T. S. D. Between December 1, 1936 and January 6, 1937 she had received a total dose of 3750 R., or 1250 R. to each portal. Between January 7 and April 30, 1937 she had a daily dosage (excepting Sundays) of 75 R.; T. S. D. 50 cm.; to three portals of entry, until she had a total dose of 5625 R., or 1875 R. to each portal.

Eighteen blood examinations were made between December 1, 1936 and May 28, 1937. Her hemoglobin varied between 70 and 80 per cent; red blood cells between 3,500,000 and 4,32,000; white blood cells between 3,400 and 7,300. Her last count on May 28, 1937 was: hemoglobin 80 per cent; red blood cells 4,000,000; white blood cells 5,200.

X-ray examinations were as follows:—On November 30, 1936 no metastases of the chest were seen. On December 3, 1936 Dr. Herendeen re-

ported marked enlargement and deformity of the left kidney. The right kidney appeared normal. Both kidneys excreted the dye, the right normally; the function of the left appeared to be limited to the lower pole.

The child was not much disturbed by her X-ray treatments. On February 9, 1937 it was difficult to find any tumor of the kidney. On March 2, 1937 no tumor could be felt and her condition was excellent. On November 17, 1937 she was gaining weight at the rate of one pound a month. She was in good condition and no tumor was palpable.

Comment. The above two cases of Wilms' tumor emphasize that with a change in the method of giving X-ray therapy the results have become semi-permanent, thus completely reversing our earlier idea of the effect of X-ray.

X-RAY EFFECT ON ADULT TUMORS

Illustrative Case. P. W., a female, aged 42, was admitted to the Memorial Hospital on July 19, 1935 with the following history. Five months ago the patient began to have pains in her right abdomen and flank. In June she had had urinary frequency and the urine became brownish in color. In July her pain in the right side became very severe. She had much vomiting. She was sent to New York Hospital and was there seen by Dr. Dean. She had at that time a somewhat tender mass in the right abdomen extending from the costal margin to one inch below the umbilicus. Her urine contained red and white blood cells and albumin. Red blood count was 3,790,000; white blood count was 13,400; hemoglobin was 70 per cent; urea nitrogen 51. Retrograde pyelogram studies showed a marked elongation of the upper calyx characteristic of kidney tumor. Uroselectan showed normal excretion on the left but was not excreted on the right. No urine came from the right kidney on ureteral catheterization and no indigo carmine after twenty minutes. The diagnosis of right kidney tumor was made.

She received at the Memorial Hospital the following X-ray treatment. Through three portals, at a distance of 70 cm. she obtained a daily dose of 300 R. Between July 19 and August 16, 1935 a total dose of 7200 R., or 2400 R. was given to each of three portals of entry.

The kidney apparently receded in size very rapidly. The pain stopped and her condition became much improved. On November 10, 1937 there was no sign of disease. The diagnosis of kidney tumor was made from the pyelogram, from the enlarged kidney and from the marked recession of the tumor under X-ray treatment. This patient has been well two years and four months since she was first seen.

POSTOPERATIVE METASTASES CONTROLLED BY X-RAY THERAPY

Illustrative Case. D. N., a female, aged 23, was admitted to the Memorial Hospital on April 21, 1934 with the history that in May 1929 an

enormous tumor of the kidney had been removed. In 1934 a laparotomy was performed for a partial intestinal obstruction; a large metastatic tumor mass was found beneath the diaphragm at the vena cava foramen.

At the time of admission a deep mass was palpated in the left upper quadrant near the midline. X-ray examination of the chest showed no metastases.

She was given X-ray therapy to the left upper abdomen through three portals of entry, anterior, posterior and lateral—300 R. daily at 70 cm. until she had a total dose of 7200 R. or 2400 R. to each portal. Her condition gradually improved, although her semi-intestinal obstruction persisted. This finally seemed to settle down to controllable constipation. The tumor disappeared. She was in fairly good shape up to February 16, 1937, when she began to go downhill. Her metastases were held in check for three years.

EFFECT OF RADIATION ON KIDNEYS REMOVED AT OPERATION— ILLUSTRATIVE CASES

Case 1. P. N., a female, aged $1\frac{1}{2}$ years, had had abdominal pain for two or three weeks. A tumor had developed in the left side of the abdomen corresponding to the site of the left kidney, with the characteristics of a Wilms' tumor. Intravenous urography revealed a marked distortion of the pelvis and calyces of the left kidney. The kidney filled the entire left abdomen. The right kidney was normal. The diagnosis was a primary tumor of the left kidney. There was no evidence of chest metastasis. Roentgen ray therapy was begun on September 21, 1936. With three portals of entry, 198 K. V., at a distance of 50 cm., 200 R. were given daily. Between September 21, and October 19, 1936 (one month) a total dose of 4400 R. was given, or 1466 R. to each portal.

The tumor rapidly decreased in size. For two weeks the patient's condition was worse. Then she began to pick up. A left nephrectomy was performed on October 22, 1936. She made an uneventful recovery. She received further X-ray treatment and on September 23, 1937 her condition was good.

The pathological examination of her removed kidney showed embryonal adenocarcinoma, Grade III, (not a typical Wilms' tumor; it contained many embryonal tubules and abortive glomeruli). No radiation changes were seen.

Comment. The operation followed quickly upon the end of the first course of irradiation, and there were obviously clinical effects of the irradiation because the kidney was markedly reduced in size. Yet these could not be identified by the pathologist.

Case 2. M. B., a female, aged $4\frac{1}{2}$ years, was admitted to the Memorial Hospital on August 18, 1934 with a history of a rapidly growing tumor of the right upper abdomen, first noticed two months before admission. She

was somewhat anemic and apathetic. She had a right abdominal tumor extending below the ribs to the iliac crest and to the umbilicus. This was diagnosed as a Wilms' tumor of the kidney. Her chest plates showed no metastases.

She was placed on X-ray therapy, receiving 200 R. daily at a distance of 50 cm. to three portals of entry– anterior, lateral and posterior. From August 21 to September 7, 1934 she received a total dose of 4600 R., or 1533 R. to each portal. She had little reaction to the therapy and her tumor decreased rapidly in size. Late in the course she did have some temperature rise.

A nephrectomy was done on October 10, 1934 and a kidney only slightly larger than normal was removed without difficulty. She recovered from the operation and went home on October 22, 1934. On November 12, 1934 she showed on X-ray examination pleural effusion of the right chest and evidence of infiltration of the parenchyma of the lung by tumor. She received X-ray therapy to her lungs and the metastasis was fairly well controlled.

On February 26, 1935 she came to the hospital complaining of twitching of her right arm and right eye. She was mentally confused. There was paresis of the right shoulder muscles; the left angle of her mouth was drawn downward. She had projectile vomiting and irregular respirations. She died that night from a brain metastasis.

The pathological report of the excised kidney, which had been previously X-rayed, was "Suppose this is embryonal carcinoma. Tumor is reduced to necrotic shadow cells. In the midst of remains of kidney alveoli are occasional areas which resemble degenerated striated muscle. This points to the tumor having been an embryonal adeno-myosarcoma. Do not think this could possibly recur locally."

Comment. The X-ray treatment had a devastating effect upon the tumor. This effect would probably have been permanent and the nephrectomy was unnecessary.

Case 3. J. J., aged 53 years, was admitted to the Memorial Hospital on May 26, 1937. For four or five years he had had difficulty in urinating. There had been some nocturia, and, six months previously, after passing urethral sounds, hematuria was noted. Since then he had had periods of hematuria. Three months before, he had felt a hard lump in his right upper abdomen.

Examination revealed a firm, non-tender, movable tumor in his right upper abdomen extending 8 cm. below the costal margin. Diodrast test showed no dye excreted from the right kidney; the left kidney was normal. A diagnosis of right kidney tumor was made.

The patient was given X-ray therapy. He was given 250 R. daily at a distance of 70 cm. to three portals of entry. From June 1 to July 12, 1937 he received a total dose of 6000 R. or 2000 R. to each of the three

portals. There was little reduction in the size of the tumor. On August 26, 1937 the right kidney was removed without trouble. He recovered from the operation and is doing well.

The pathological examination of the kidney, which had been previously radiated, was "hypernephroma." Aside from extensive cystic degeneration, there were no changes attributable to radiation.

Comment. Had the nephrectomy been deferred longer, the radiation changes might have been greater. This is a type, however, that is radio-insensitive.

DISCUSSION

Dr. Ewing, in a personal communication, has discussed the variation between the radiation effect upon Wilms' tumors of the kidney and embryonal tumors of the testicle from a pathological standpoint. He said:

"A considerable number of observations have been made that there is a marked difference in the reaction to radiation between embryonal carcinoma of the testis and Wilms' tumor of the kidney, although both are embryonal tumors. After full doses of X-ray the carcinoma of the testis regresses promptly and very rarely recurs, while after similar treatment the Wilms' tumors regress, but not completely, soon recur locally and eventually cause the death of the patient. On examination of these tumors after radiation, it is found that the carcinoma of the testis presents a structure of uniform anemic necrosis involving all the tumor cells, and the necrotic tumor tissue is replaced by a type of edematous granulation tissue. After similar treatment the Wilms' tumor shows massive areas of hemorrhagic necrosis, but outlying lobules of the tumor survive and may show little effects of radiation. It appears probable that this striking difference depends on the difference in the character of the blood supply in the two tumors. The testicle tumor is a histoid neoplasm growing diffusely and receiving its nutrition from a series of fine capillaries which are easily affected by radiation, which occludes the vessels and shuts off the blood supply. The Wilms' tumor, on the other hand, is an organoid neoplasm, composed of many lobules receiving nutrition through a series of arteries which supply the lobules and ramify like the branches of a tree. Such vessels are less readily affected by radiation. When such vessels are exposed to radiation some may be occluded with the resulting hemorrhagic necrosis, but others, more resistant, maintain the circulation and the tissue they supply survives. While both tumors receive heavy doses of radiation and both are comparatively radiosensitive, the necrosis in both instances is probably due for the most part to the shutting off of the blood supply. It is a general rule in pathology that extensive necrosis of tissue is nearly always due to obstruction of the blood supply.

Recently it has been found that if the radiation of Wilms' tumors is continued over a long period the tumor may be controlled and does not

recur. This result may probably be referred to the gradual obliteration of the lumen of the more resistant blood vessels accomplished slowly by a long course of deep radiation. There are indications also, that the cells of the embryonal carcinoma of the testis are more radiosensitive than those of the Wilms' tumors, some of which show considerable differentiation toward the adult type. If this assumption is correct then it forms another indication for the prolonged program of radiation of the Wilms' tumors, aiming at growth restraint and the gradual shutting off of the supply of blood. In neither case may the curative result be safely referred to the direct effects of the rays upon the tumor cells.

The above hypothesis is offered as a probable explanation of the course of radiation therapy in these two types of tumors, and as an argument in favor of prolonged radiation of the Wilms' tumors, but the conditions in the tumors are quite complex, and the suggestion offered can hardly be regarded as fully proven."

SUMMARY

The several observations on the effect of roentgen therapy on kidney tumors indicate that in roentgen therapy we have possibly a more efficient agent than it has been previously believed. In Wilms' tumors the regression may be permanent if the roentgen therapy is given in a series of very small daily doses and continued over a long period of time.

URETERAL OCCLUSION FOLLOWING RADIUM IMPLANTATION INTO THE CERVIX

Further Observations

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During 1934, the writer reported (1) a series of cases in which ureteral occlusion had followed irradiation for carcinoma of the cervix. These cases, eight in number, were all observed at the Woman's Hospital. In six of the eight cases, the writer did a nephrectomy, a functionless kidney, free of metastasis, being removed in each instance. In the seventh case there was a bilateral obstruction of the ureters, and in case eight the presence of extensive metastasis prohibited operation. Microscopic sections of the ureters in the two cases not operated but studied post mortem, showed the presence of carcinoma and fibrosis in the ureteral wall. These eight cases are summarized as in Table 1.

The follow-up of these cases shows that all are dead.

Case 1—Died following an operation for intestinal obstruction, 15 months after nephrectomy

Case 2—Died 24 months after nephrectomy, cause unknown

Case 3—Died 39 months after nephrectomy, cause unknown.

Case 4—Died of pneumonia, 5 years after nephrectomy.

Case 5—Died of general metastasis, 5 months after nephrectomy.

Case 6—Died one week after nephrectomy. General metastasis.

Case 7—Not operated. Post mortem showed general metastasis.

Case 8—Not operated. Post mortem showed general metastasis.

None of these cases had a urinary infection or presented urinary symptoms when radiation was started. All had negative Wassermanns. Tissue removed at biopsy in each case showed squamous cell carcinoma.

Since 1934, eight additional cases have been referred to the Urological Clinic presenting symptoms attributable to the urinary tract, all patients being treated by irradiation for carcinoma of the cervix. In seven, radium was employed; the eighth is now being treated with deep X-ray therapy, while another case had a Wertheim operation. These recent cases may be summarized as in Table 2.

None of the eight cases in this last series presented urinary symptoms; and all had negative urinalyses when radiation was commenced. The Wassermann was negative in each case. A biopsy was taken on all of these cases, the sections showing squamous cell carcinoma.

In the first case of this series, although no ureteral occlusion was encountered, the urogram (Fig. 1) shows a right hydronephrosis. The first urogram (Fig. 2) of the second case shows no ureteral occlusion, while the second urogram (Fig. 3), made four months later, shows, even in the apparent absence of ureteral obstruction, a right hydronephrosis. In the third case neither ureteral orifice was visualized, urinalyses were negative, and the urogram (Fig. 4) shows a left hydronephrosis, the right kidney having emptied completely. The fourth case presented a right hydronephrosis (Fig. 5) with a stricture of the ureter. The first urogram (Fig. 6) in the fifth case shows a beginning dilatation of the right ureter, while the second urogram (Fig. 7), taken nineteen months later, shows a well marked hydronephrosis and hydroureter. In cases six and seven, in both of which there was an atrophy of the urethra, the urograms (Figs. 8 and 9) show a hydronephrosis on one side, the opposite kidney having emptied com-

TABLE 1

	MILLIGRAM HOURS OF RADIATION	ONSET OF URINARY SYMPTOMS	UROLOGICAL LESION
1	2428.8	22 months after radiation	Stricture of ureter, uretero-vaginal fistula
2	1787.5	7 months after radiation	Stricture of ureter, uretero-vaginal fistula
3	4857.68	5 months after radiation	Stricture of ureter, uretero-vaginal fistula
4	3146.88	7 months after radiation	Stricture of ureter, uretero-vaginal fistula
5	4242.24	22 months after radiation	Stricture of ureter, uretero-vaginal fistula
6	3580.8	9 years after radiation	Stricture of ureter, uretero-vaginal fistula
7	2426.89	1 month after radiation	Stricture of both ureters
8	Vaginal and surface packs	5 years after radiation	Vesico-vaginal fistula

pletely. In case nine, there is a right hydronephrosis, the left kidney having emptied completely (Fig. 10). Among these recent cases there was no instance of a complete ureteral occlusion, nor of a ureterovaginal fistula.

Although cases one and two showed a hydronephrosis, the symptoms presented did not warrant a nephrectomy. In case three, the patient's condition contra-indicated a nephrectomy. The fourth patient refused operation. In the fifth case a nephrostomy was done, the patient's condition contra-indicating a nephrectomy. The sixth patient had general metastasis, the hydronephrosis causing no apparent symptoms. The seventh patient (82 years of age) had no symptoms relative to the hydronephrosis, while the two last cases are still under observation.

Unfortunately, the four patients of this last series who succumbed, died in another hospital and a post mortem examination was not obtained.

During the past three years attention has been focussed more closely

TABLE 2

CASE	AGE	DATES OF TREATMENT	MILLIGRAM HOURS	ONSET OF URINARY SYMPTOMS	SYMPTOMS	UROLOGICAL FINDINGS	OUTCOME
1. S. J.	58	8/30/33 2/ 7/34	Total 4168.8	8/14/34	Difficulty in voiding. Pain in right lower quadrant	Stricture of urethra. Retention 30 ounces. Elevation of bladder base. No obstruction of ureters. Indigo carmine 4 minutes on left side. No return on right. Specimens normal. Urogram—right hydronephrosis	Died 10/8/34
2. G. R.	52	10/18/33 6/13/34	Total 5293.2	8/ 1/34	Frequency, dysuria. Pain in left lower quadrant	Stricture of urethra. Congestion of bladder base. No ureteral obstruction. Urine negative. Urograms 8/1/34 and 12/18/34	10/10/34, resection of ileum. Died 3/20/35
3. J. M.	51	10/26/34	1200	1/26/35	Frequency, nocturia. Pain in both lower quadrants	Edema of base of bladder. Ureteral orifices not observed. Urine negative. Urogram—left hydronephrosis	Died 4/7/35
4. M. R.	65	9/28/25 10/11/25 10/ 6/35	Total 3628.8	4/20/35	Pain in right lower quadrant	Congestion of base of bladder. Obstruction of right ureter at 18 cm. Left urine negative. Urograms—Calcified fibroid. Right hydronephrosis	Refused operation
5. M. G.	49	Wortheim operation 6/5/35		6/21/35	Dysuria. Frequency	6/21/35 Congestion of bladder base. No obstruction of ureters. Urines sterile. Urogram—Right hydronephrosis. 5/20/37—Right hydronephrosis. 5/22/37—Nephrostomy	10/2/37, general metastasis
6. M. Z.	49	10/25/29	3600	8/13/30, vesicovaginal fistula;5/9/36, to clinic	Incontinence. Pain in left upper quadrant	Atrophy of urethra. Cystoscopic examination not possible. Urograms—Hydronephrosis on right side	Died 3/18/37

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	Age		Total				
7. J. M.	82	9/11/20 11/19/20	4873.44	5/20/25, ves-icovaginal fistula; 10/24/36, to clinic	Incontinence	Atrophy of urethra. Cystoscopic examination not possible. Urograms—Hydronephrosis on left side	7/17/37, last seen. Incontinence only
8. M. O.	48	7/10/36	4200	9/11/37	Frequency. Dysuria	Congestion of bladder base. Colon bacillus infection and calculi in right kidney	Operation for cancer of breast 10/20/37. Right nephrectomy later
9. V. S.	28	Advanced carcinoma of cervix and vagina. Not suitable for radium. Treated by X-ray		10/23/37	Pain in left upper quadrant	Edema and congestion of bladder base. Left ureteral orifice not visualized. Right ureter and urine negative. Urogram—Right hydronephrosis	Shall radium be given later?

Fig. 1. Right hydronephrosis

Fig. 2

Fig. 3

Fig. 2. Negative urogram

Fig. 3. Right hydronephrosis; left kidney has drained completely

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FIG. 4   FIG. 5

FIG. 4. Left hydronephrosis; right kidney has drained completely
FIG. 5. Right hydronephrosis above stricture of ureter

FIG. 6   FIG. 7

FIG. 6. Early dilatation of the right ureter
FIG. 7. Hydronephrosis nineteen months later
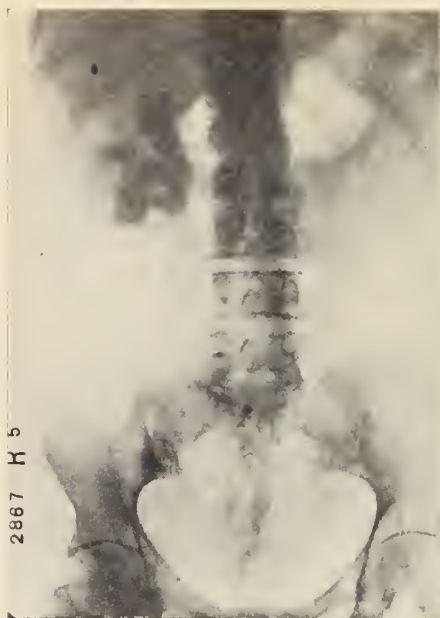
FIG. 8   FIG. 9

FIG. 8. Right hydronephrosis; left kidney has drained completely
FIG. 9. Left hydronephrosis; right kidney has drained completely

FIG. 10. Right hydronephrosis; left kidney has drained completely

upon the urinary tract, during and after treatment of carcinoma of the cervix by irradiation. It is possible that these more recent cases in which a hydronephrosis has been demonstrated in the absence of complete occlusion of the ureter, represent an early stage of ureteral obstruction, the patients succumbing to the disease before the obstruction becomes complete.

The results obtained by irradiation have continued to be such as to warrant its general employment in the treatment of carcinoma of the cervix. Urological complications apparently occur late in the course of the disease; it is questionable, however, if they shorten the life of the individuals, in all of whom there is evidence of metastasis at the time of their appearance.

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ALKAPTONURIA

With Case Report

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Alkaptonuria was first described by Boedeker (1) in 1861. Alkapton is derived from two Greek words, the first meaning alkali, and the second, to absorb quickly.

It is a rare disease. Bagnal (2) in 1929 stated that only one hundred and twenty-six cases had been reported, and that his was the seventeenth in the American literature. It is not distinctly hereditary, but shows a familial tendency, especially in consanguineous marriages.

Garrod's (3) eleven cases occurred in four families—in all of these the parents were first cousins. Anderson (4) in 1922 describes in detail one case and reports two others in the same family. The condition is due to a freak of metabolism in which the amino acids, tyrosin and phenylalanine, are not converted into their end products. Gibson and Howard (5) gave one of the best available descriptions of the chemical changes in the condition (Fig. 1). They went on to state that if tyrosin and/or phenylalanin were given to an alkaptonuric, a corresponding amount of alkapton would be eliminated, but when these were given to a normal person they were converted into their end products, and hemogentisic acid would not be found in the urine. This error of metabolism is complete and maximal in that the ratio of hemogentisic acid bears a very definite relation to the total nitrogen. The cause of alkaptonuria has not been definitely determined. In a very recent article by Klein and Block (6) it was demonstrated that the intramuscular injection of liver extract completely freed the urine of homogentisic acid after four to six hours, and for a duration of eight to ten hours. This may point the way for further studies that may explain this metabolic disorder.

Most of the reported cases have started in infancy, or have been noted over a period of years. There seems to be little, if any, disturbance of general health. Several cases of ochronosis have been reported; in these alkaptonurics, blackish deposits in bone, costal and aural cartilages, have been found. The deposits in the ear can be seen as darkish areas, especially upon transillumination. Pain in the affected parts had been noted. Brutenfelder (7) gave a good description of a case of ochronosis alkaptonuria. Albrecht (8) thought that these blackish deposits were due to a combination of homogentisic acid with chondromucoid of the cartilages but this does not explain similar deposits in bone.

Alkaptonuria is usually discovered by the color of the urine after it has been standing, black stains on diapers and under clothes, or a false sugar reaction with Benedict's, or Fehling's solution. Alkaptonuria has been, at times, erroneously diagnosed as diabetes and so treated, naturally without improvement. Correct diagnosis could have been made by doing a fermentation, a polariscopic, or a blood sugar examination, as homogentisic acid does not ferment, and does not cause rotation of polarized light.
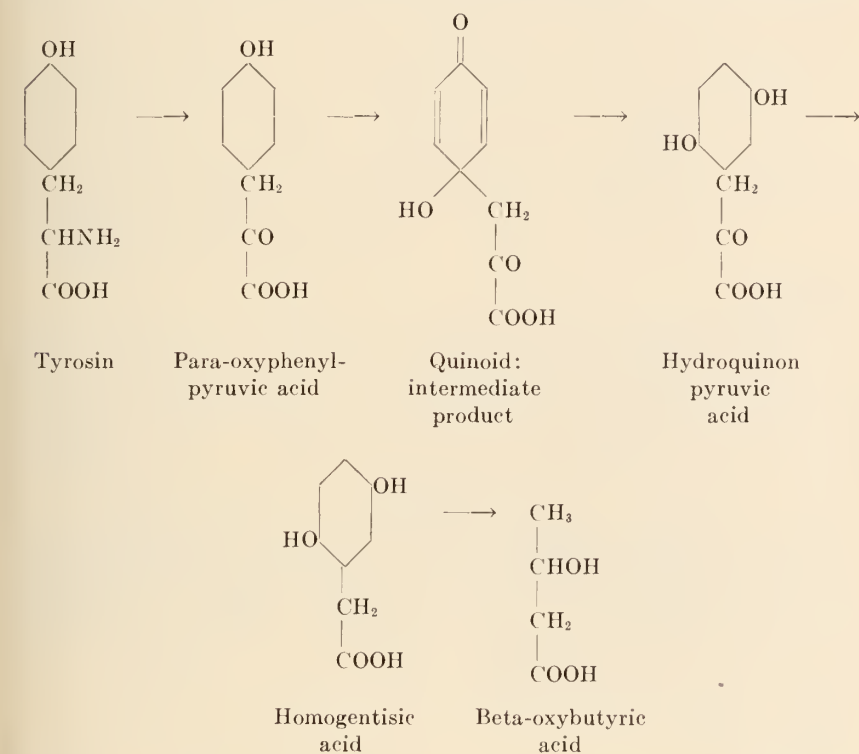
FIG. 1. Scheme of origin of homogentisic acid (adapted from Neubauer; Gibson and Howard)

The tests for homogentisic acid are (Anderson (4)):

1. Upon exposure to air, or the addition of alkali, the urine turns brown, and gradually black.

2. It reduces copper solutions.

3. It does not reduce alkaline bismuth solution (Nylander's reagent)

4. It does not react to the fermentation test.

5. It does not rotate polarized light.

6. It reduces silver lactate, the reagent of Folin and Wu, in the cold, which no other reducing substance in the urine will do.

7. Upon the addition of a dilute solution of ferric chloride, a deep blue color appears for a moment until oxidation is complete.

CASE REPORT

On January 14, 1929, a married, nulliparous patient brought in a specimen of urine containing some peculiar looking crystals, which Dr. O. S. Hillman did not think belonged to any known type of urinary crystals. There was also an interlacing network of fiber-like material, jet black in color, which seemed to be of vegetable origin. Occult blood was negative. Two days later she produced another specimen of a slightly pinkish tinge, containing vegetable matter of extraneous origin. The cause of the color was not determined. As she claimed it had been passed without contamination, the presence of the vegetable matter could not be accounted for. Careful examination ruled out any possibility of a vesico-intestinal fistula. The patient was markedly neurotic, and the idea of deception was entertained.

On January 22nd, she stated that the morning urine had been black; but a catheterized specimen in the forenoon was clear. She then made the observation that if she voided during the early morning hours, the urine was clear, but if she slept until eight or nine o'clock without emptying the bladder, the first specimen passed would be black. This gave the clue that the elements of time and heat (body warmth) were conducive to bringing out the color. A clear specimen was incubated and after a few hours it turned dark. Alkaptonuria was suspected and a specimen was sent to Dr. F. E. Sondern, who reported that the color was not explained by silver salts, alkapton, urobilin, uroerythrin, or melanin. A specimen was sent to Alexander O. Gettler, Ph.D., New York City toxicologist, whose detailed report is as follows:

Reaction: Acid.
Albumen: Absent.
Sugar: Absent
Acetone: Absent.
Blood: Absent.
Diacetic acid: Absent.
Bile: Absent.
Special Tests:
Fehling's: Gives a pseudo reaction.
Nylander's: Gives no reaction.
Millon's: Gives a pink color, which on heating gives a bright red precipitate.
Mercuric Chloride gives a ppt. which on heating gives no red.
Nitroprussic Test gives no indication of melanin.
Phosphotungstic Test gives a deep blue color, far deeper than normal urines.
Ferric Chloride Test is negative. even on distillate.
Silver is absent.
Arsenic trace.
No other heavy metals present.

Conclusion: The Millon's test, and the Phosphotungstic test indicate to me, that there is some abnormal tyrosine metabolism present. The tyrosine is evidently excreted as a polypeptide, perhaps joined to homogentisic acid.''

This condition prevailed until the latter part of February 1929. In March 1929, she had clay-colored stools and her icteric index was 17.8, but the urine was then free of the black color, and she did not have a recurrence of the condition while under my observation.

This patient had had many operations. In 1921, she had a round ligament shortening, appendectomy, and right salpingo-oophorectomy; in 1926, cholecystectomy; in 1928, freeing of omental adhesions to the abdominal wall, freeing of the uterus from the anterior abdominal wall, hysterectomy for fibroids, and left salpingo-oophorectomy.

Her urine constantly contained a few red blood cells, but evidence of renal or bladder growth, stones or tuberculosis, could not be found by thorough urological examination.

It is doubtful whether this should be considered a case of true alkaptonuria, or just a closely related one. Its brief duration is against the general rule of the permanence of true alkaptonuria, and there was a failure to secure a complete alkaptonuric reaction with some of the tests. Undoubtedly the phenomenon was due to some abnormal metabolism of tyrosine.

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BALANCED SUSPENSION IN FRACTURES OF THE SHOULDER

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The treatment of impacted fractures of the shoulder with more or less fragmentation, tearing off the greater tuberosity, etc., has received considerable attention from time to time. Often these were treated by immobilization in a Velpeau bandage with suitable padding in the axilla, etc. A stiff shoulder joint usually followed three weeks' immobilization in this position.

To avoid this effect, airplane splints were employed to immobilize the fractured shoulder in abduction, the forearm lying horizontally on the splint. With this position external rotation was lost.

It was then realized that, in addition to abduction of the shoulder at right angles, the forearm should be kept vertical. The results were better because, even if the shoulder joint was somewhat stiff, the scapula rotated upon the thorax as the elbow came down to the side.

For the past few years the author has employed balanced suspension of the upper extremity to retain function from the very beginning.

The method is simple. The patient is laid in bed. Strips of moleskin adhesive plaster, applied to the dorsal and palmar aspects of the forearm, are attached to a spreader and cord leading to suitably placed pulleys and counter weights, just enough weight being applied to have the upper arm swung horizontally, clear of the bed. The forearm being vertical, the overhead point of suspension is directly over the point of the elbow. The elbow itself is to be carried away from the side abducted as far as the patient's comfort permits (Fig. 1).

The patient is instructed to practice abduction and adduction within the limits of pain. In addition, physical therapy from the onset has been found most useful in relieving local pain and increasing the range of active motion.[1] The range of voluntary motion increases day by day. The average time of stay in bed is about three weeks.

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[1] The physical therapy consists of infra-red radiation at twenty to thirty inches distance, depending on the strength of the infra-red generator, given at frequent intervals daily to the limb for thirty to forty minutes at a time. Between such treatments the limb must be kept covered to maintain warmth. A very delicate massage to the limb, not over site of fracture, is given daily. Active exercise distal to the site of fracture and within the limits of pain, is maintained from the outset. The patient is instructed to keep up active motion, within the limits of pain, at frequent intervals during waking hours. Only when the patient can abduct the limb in erect posture is physical therapy to be discontinued.

At the end of two weeks the patient is allowed up and about with his arm in a sling, when suspension is discontinued at intervals during the day. At night it is resumed.

Eventually 90°
voluntary motion
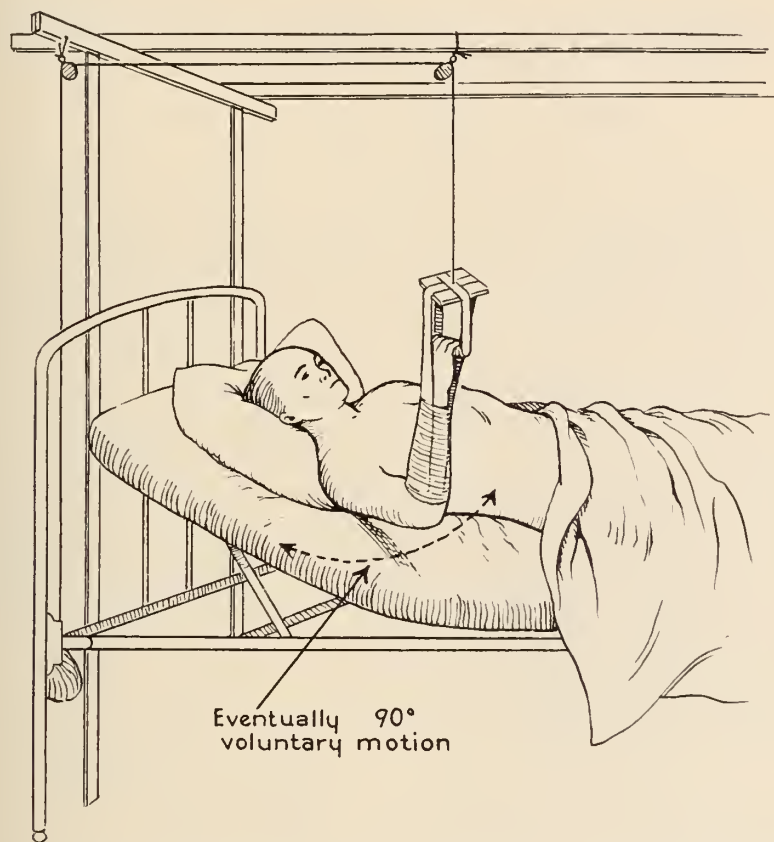
Fig. 1. Balanced suspension for impacted fractures of the shoulder. Sufficient weight counterbalances the upper extremity, permitting the upper arm to swing clear of the bed, and allowing active motion within the limits of pain, with minimal muscular effort.

Skin traction is removed at the end of about three weeks but the abducting exercises in balanced suspension, with patient lying flat on his back, are continued by placing the elbow and forearm in a sling properly counterbalanced. These exercises are continued until complete range of motion in the erect posture has been attained.

ANOMALIES OF KIDNEY AND URETER AS THE CAUSE OF SURGICAL CONDITIONS

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Anomalies in the upper urinary tract are more commonly observed than in any other system of the body. In olden times anomalies were rarely discovered even post mortem, owing to the difficulty of obtaining material for anatomic dissection and to the lack of proper methods of investigation and diagnosis, as a result of which these malformations were long considered as anatomic curiosities. Since Albarran's systematization of the use of cystoscopy and catheterization of the ureters, and the discovery of pyelography, and more recently the introduction of intravenous urography, it has been possible to diagnose innumerable malformations and pathologic conditions of the kidney that were never before suspected. So amazing is the rôle of the vast number of anomalies of the urinary tract in the etiology of diseases and surgical conditions, as recognized in this urographic era, that it can safely be said that fully 40 per cent of all pathologic conditions of the kidneys and ureters are due to congenital anomalies, and that these malformations constitute the most extensive chapter in modern urology.

While it is true that not every such anomaly constitutes a pathologic lesion with clinical symptoms, it has nevertheless been demonstrated·by modern urology that any congenital abnormality is potentially a clinico-pathologic entity and liable to become a surgical condition. Such anomalies predispose to poor function and to urinary stasis with resultant retention and possible infection. In many cases of chronic pyuria and recurrent attacks of pyelitis or nephritis in children, the underlying cause has been found to be a congenital malformation of the urinary tract. Deficient function, nephritis and pyelonephritis, as well as hydronephrosis and calculus, are of common occurrence in kidneys that are congenitally abnormal; and in cases in which only one kidney shows an abnormality, the opposite kidney, though normally developed, may suffer from the additional functional strain imposed on it. Fused kidneys of various types, and especially horseshoe kidney, are usually associated with some degree of ectopia, and with abnormalities in the pelvis and the form or number of the ureters. They are, therefore, frequently the site of pathologic lesions. Abnormalities of the pelvis and ureter favor obstruction

with the development of hydronephrosis, often with superimposed infection, forming pyonephrosis. In fact, one of the most frequent causes of hydronephrosis is an anomaly of the ureter or its orifices, or displacement or angulation of the ureter caused by aberrant renal blood vessels. When the malformation is in the lower portion of the ureter, it results in hydroureter as well as hydronephrosis, and, when there is infection, in pyohydro-ureteronephrosis.

These various pathologic lesions in abnormal kidneys may cause a wide variety of urologic symptoms that direct attention to the urinary tract and bring the patient to the urologist. Renal pain is of frequent occurrence in some of these conditions, occurring more frequently in kidneys with congenital abnormalities than in similar pathologic lesions in otherwise normal kidneys. However, in some instances the development of pathologic lesions in congenitally abnormal kidneys is relatively silent; that is, accompanied by few or no urologic symptoms. The patients suffer from various gastro-intestinal symptoms suggesting a lesion of some abdominal or pelvic organ or a functional disturbance of the gastro-intestinal tract. These symptoms are to be attributed to pressure or traction on other organs or nerve plexuses by the abnormal kidney. Often one or more abdominal operations have been performed without relief before the patient is referred to the urologist. It is of paramount importance, in order to avoid errors in diagnosis, that careful cystoscopic and urographic study should be made in every case in which the slightest urinary symptoms become manifest, because it is obvious that many silent surgical conditions of the upper urinary tract confuse the preoperative diagnosis and such a urologic study will often show the presence of a congenital abnormality of the kidney or ureter as the underlying cause of the entire syndrome.

In a recent communication presented before the Urological Section of the American Medical Association at New Orleans, I reported several cases of congenital absence of one kidney, as well as hypoplastic and aplastic kidney, and more recently in a monograph I have discussed the clinical management of horseshoe kidney at length. At this time, I will only report three unusual cases of anomalies of the upper urinary tract, which will serve to bring out the importance of the rôle of such anomalies in the causation of surgical conditions.

The literature on anomalies of the kidneys and ureters is so extensive and the types of anomalies are so innumerable that it would be impossible to discuss all of them in detail, and therefore for practical use I have worked out an anatomic and clinicopathologic classification to outline briefly the various types of congenital abnormalities of the kidney, its excretory apparatus (calices, pelvis and ureter) and its blood and lymphatic supply. This classification is given in the accompanying tables.

EMBRYOLOGY

The term "congenital anomalies" implies that the origin of such anomalies is to be sought in embryonic life. A study of the development of the urogenital system shows its great complexity and indicates the reasons for the wide diversity of types of congenital malformations in the upper urinary tract. In the embryologic evolution of this tract, three essential renal organs are formed in rapid succession, the pronephros, the mesonephros and the metanephros; only the latter persists to become the kidney. In the course of the kidney's development it undergoes a migration upward, when the ureter, increasing in length, forces the renal anlage to change its position, the caudal extremity rising more slowly. Not only does the kidney migrate; it also undergoes a rotation around its longitudinal axis.
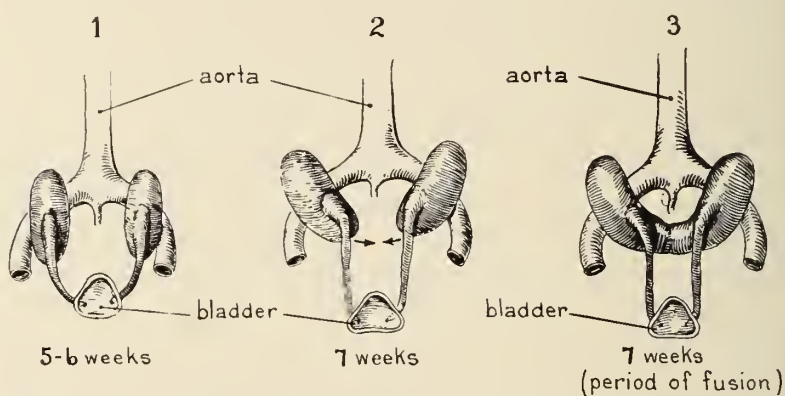
Fig. 1. Diagrammatic drawing showing the different stages of ascent, rotation and migration of the kidneys during embryonic life, and revealing the theoretical occurrence of fusion to form the horseshoe kidney. (From Gutierrez, Robert: The Clinical Management of Horseshoe Kidney, New York, Paul B. Hoeber, Inc., 1934.)

Because of the intimate relation of the kidney to the umbilical arteries and the bifurcation of the aorta, it is evident that there may be some mechanical obstruction by these arteries to interfere with the kidney's migration and rotation (fig. 1). Such interference would result in various types of fused and ectopic kidneys, fusion being due to the union of two kidney blastomas in early fetal life. The fused organ may assume a number of different shapes and may be symmetrical or asymmetrical with reference to the midline of the body. Most important of these types of fused kidney is the horseshoe kidney, in which the two renal organs have become fused into a single mass lying directly across the median axis of the body, joined together by an isthmus. Such fused kidneys are usually also ectopic.

TABLE 1

Anomalies of the Kidney Proper

1. Anomalies of Number
   (a) Absence of both kidneys
   (b) Absence of one kidney (solitary kidney)
   (c) Double or multiple kidney (supernumerary kidney) $\begin{cases} \text{Unilateral} \\ \text{Bilateral} \end{cases}$

2. Anomalies of Size
   (a) Hypoplastic kidney $\begin{cases} \text{True renal hypoplasia} \\ \text{Renal aplasia} \end{cases}$
   (b) Hypertrophic kidney $\begin{cases} \text{Lobulated} \\ \text{Compensated} \end{cases}$

3. Anomalies of Form
   (a) Long kidney
   (b) Short kidney
   (c) Broad kidney
   (d) Lobulated kidney
   (e) Cystic kidney $\begin{cases} \text{Unilateral} \\ \text{Bilateral} \end{cases}$
   (f) Polycystic kidney $\begin{cases} \text{Unilateral} \\ \text{Bilateral} \end{cases}$
   (g) Fused kidney
      - Asymmetrical
         - L-shaped kidney
         - Sigmoid kidney
         - Ring-shaped kidney ("en gallette")
         - Kidney en masse
      - Symmetrical (horseshoe kidney)
         - With concavity above
         - With concavity below
         - With fibrous isthmus
         - With isthmus of true renal parenchyma
         - With one, two, three or four pelves and ureters

4. Anomalies of Position
   (a) Movable or floating kidney
   (b) Ectopic kidney $\begin{cases} \text{Simple unilateral} \\ \text{Simple bilateral} \\ \text{Bilateral with fusion (horseshoe kidney)} \\ \text{Crossed with or without fusion} \end{cases}$

   Any of these anomalies of position may be $\begin{cases} \text{Lumbar} \\ \text{Iliac} \\ \text{Pelvic} \\ \text{Median} \end{cases}$

5. Anomalies of Rotation
   (a) Deficient rotation $\left.\begin{matrix} \\ \end{matrix}\right\}$ $\begin{cases} \text{Unilateral} \\ \text{Bilateral} \end{cases}$
   (b) Excessive rotation

If for any reason the elements of the Wolffian duct are arrested in their development of the primitive nucleus on one side, half of the urinary apparatus will be absent from the earliest period of fetal life. The same

general embryonal influences that interrupt the orderly development of the kidneys may also be responsible for the various anomalies of the pelves

TABLE 2

Anomalies of the Excretory Apparatus of the Kidneys (Calices, Pelvis and Ureter)

1. Calices
   - Absent
   - Aberrant
   - Abnormal in number, size or position

2. Renal pelvis
   - Absent
   - Rudimentary
   - Double (bifid) or multiple
     - Unilateral
     - Bilateral
   - Hydronephrosis (congenital)
     - Intrarenal pelvis
     - Extrarenal pelvis
       - Unilateral
       - Bilateral
   - Diverticulum of renal pelvis

3. Ureter
   - Anomalies of number
     - Single (one ureter absent)
     - Double on one side
     - Triple
     - Quadruple
       - Complete
       - Incomplete
     - Quintuple
     - Sextuple
   - Anomalies of form, size and position
     - Diverticulum of ureter
       - Simple
       - Multiple
     - Imperforate ureter
     - Stricture of the ureter
       - Pyo-ureter
       - Hydro-ureter
       - Megalo-ureter
     - Dilatation of ureter
       - Total
       - Partial
     - "Golf hole" type of ureteral orifice
     - Ureter ectopic
       - Misplaced in bladder
         - At fundus
         - In diverticulum
         - Near bladder neck, etc.
       - With extravesical orifice opening into
         - Other ureter
         - Urethra
         - Genital tract
         - Bowel
     - Ureters crossed
       - With renal fusion
       - In ectopia without fusion
       - Unilateral transverse
       - Bilateral transverse
     - Ureter twisted or occluded
     - Ureter twisted around vena cava
     - Ureter with valve formation
     - Ureterocele

and the ureters. There may be a surplus, a deficit or an ectopia of the excretory passages, depending on the precise nature of the developmental abnormality in the ureteral bud in very early fetal life.

SYMPTOMATOLOGY

When any congenital anomalies of the urinary tract are present, the individual may reach adult age without having any clinical symptoms indicating their existence; but this is rather unusual. Sometimes it is the effect of a general constitutional disease that causes symptoms to develop by putting additional strain on the working capacity of the kidneys. It is therefore the rule rather than the exception for patients with urinary tract anomalies to develop symptoms that sooner or later bring

TABLE 3
Anomalies of the Blood and Lymphatic Supply of the Kidney

1. Arteries
- Anomalies of number: 1 to 6 per kidney
- Anomalies of origin, from
  - Aorta
  - Spermatic artery
  - Common iliac artery
  - External iliac artery
  - Internal iliac artery
  - Sacral artery
- Anomalies of course with reference to
  - Vena cava / Iliac artery — Anterior / Posterior
- Anomalies of penetration at
  - Hilus
  - Superior pole
    - From renal artery
    - From aorta
  - Inferior pole
    - From renal artery
    - From aorta
    - From common or external iliac artery
  - Front or back of kidney
  - Margins of kidney

2. Veins
- Abnormal position of inferior vena cava, on left side
- Retro-aortic anastomosis of veins
- Presence of a vein at superior pole
- Presence of a vein at inferior pole opening into
  - Renal vein
  - Vena cava
  - Iliac vein
- Renal vein entirely retropyelic
- Anomalous connection with other systems

3. Lymphatics
- Following anomalous blood vessels
- Abnormally connecting with Pecquet's cistern

them to the urologist. But before they reach the urologist, a considerable proportion—probably 30 to 40 per cent—have undergone unnecessary operations because the symptoms suggested disease of some abdominal or pelvic organ. In some types of renal abnormalities, abdominal pain of an indefinite nature is an important factor in the clinical syndrome. In some cases it is associated with definite urinary symptoms which suggest—or should suggest—a lesion of the urinary tract. In others the abdominal symptoms overshadow the urinary symptoms so that the latter escape

notice unless a careful study of the patient is made. In some cases of hypoplastic or aplastic kidney there may be an entire absence of urinary symptoms and a history of bilateral abdominal pain, or there may be lumbar pain and symptoms of chronic nephritis. Even in cases of hydronephrosis, symptoms of gastro-intestinal disturbance may predominate or tumor formation may be the only symptom. In other cases there may be only slight frequency or dysuria, while in still others there may be severe renal colic and bladder distress or tenesmus, accompanied by chronic cystitis or chronic pyelitis.

HORSESHOE KIDNEY SYNDROME

One of the most characteristic clinical syndromes is that which is associated with horseshoe kidney disease, in which there are always associated anomalies of the pelves and ureters and of the blood vessels
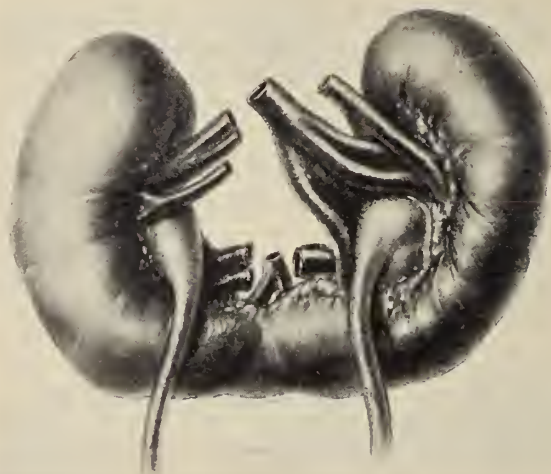
FIG. 2A. Drawing of a post mortem specimen showing a horseshoe kidney with typical fusion of the two kidneys by the lower pole.

(fig. 2). This is characterized by three main clinical features: (1) abdominal pain about the epigastric or umbilical region, (2) a history of chronic constipation associated or not with gastro-intestinal disorders and (3) urinary disturbances with early signs of chronic nephritis. This constitutes the horseshoe kidney syndrome, which I have observed in 96 per cent of my series of more than thirty cases of horseshoe kidney (and which also has been observed independently by Sangree and his associates, Foley, Papin and others). As frequently the abdominal symptoms may in the early stages of this syndrome be the predominating ones, there may often be a history of a considerable period of illness with incorrect diag-

nosis and treatment before the patient comes to the urologist. Such
patients may be acutely ill with pyelonephritis and nephritis and may
even show uremic symptoms; others have renal colic due to calculi, re-
sulting from slowly increasing urinary stasis. Some patients, however,
are referred to the urologist for less advanced urinary symptoms such as
albuminuria, microscopic hematuria, pyuria or hazy or cloudy urine with
slight pollakiuria. The abdominal symptoms are due to the fixation of
the horseshoe kidney and to its abnormal relations to the surrounding
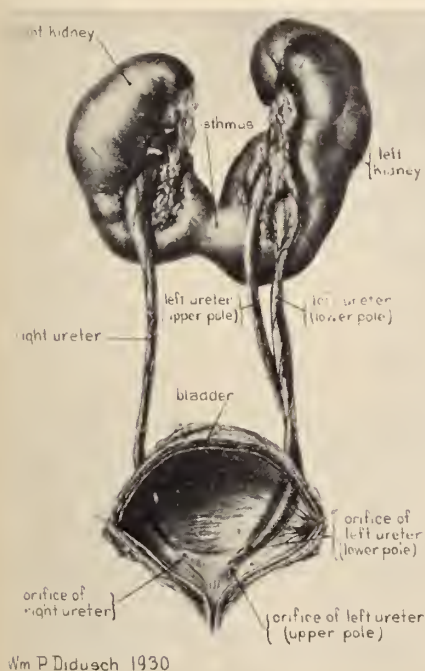
FIG. 2B

FIG. 2C

FIG. 2B. Drawing of a post mortem specimen showing horseshoe kidney with
three ureters.

FIG. 2C. Drawing of a post mortem specimen showing horseshoe kidney with
fusion by the upper pole.

organs, nerves and blood vessels. The urinary symptoms are due funda-
mentally to lack of renal drainage with resulting infection and inflamma-
tion, all directly traceable to the presence of the major renal anomaly
(fig. 3).

DIAGNOSIS

Because of the confusing nature of the clinical symptoms in renal
anomalies, a most careful and searching diagnostic study is necessary to

determine the true nature of the pathologic condition present. After a study of the patient's history, the clinical symptoms and the physical examination, the urologic examination should include cystoscopy, catheterization of the ureters, a renal functional test, roentgenography, pyelography and intravenous urography, and sometimes cystography and pyeloscopy. Cystoscopy shows lesions in the bladder, and what is of special interest in relation to urinary tract anomalies, any anomalous position of
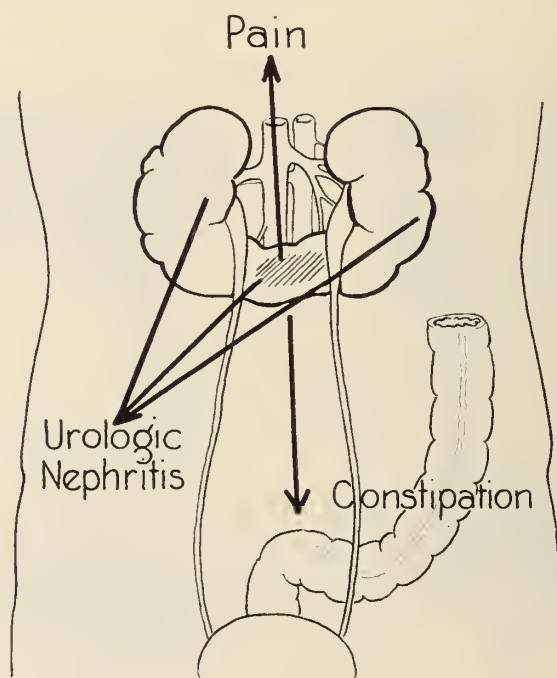
Horseshoe Kidney Syndrome

Fig. 3. The clinical syndrome of horseshoe kidney disease, showing graphically the triad of symptoms composed of (1) pain in the epigastrium or umbilical region, (2) chronic constipation, and (3) urinary symptoms of pyelitis, pyonephritis and chronic nephritis.

the ureteral orifices or anomalies of the trigone. A red and congested mucosa in the bladder may result from the infection of the urinary stasis characteristic of horseshoe kidney or anomalies of the ureter or pelvis. Chromocystoscopy may be employed, the time being noted of the first appearance at each ureteral orifice of a dye, usually indigo carmine, injected intravenously; this indicates the relative function of the two kidneys. Other functional tests should be employed and the urine from each kidney collected separately whenever ureteral catheterization is

possible. Catheterization of the ureters is an important means of re-vealing obstruction or ectopic conditions in the ureters, which are so frequently associated with malformations or ectopia of the kidneys.

In roentgenography, catheterization of the ureters with opaque catheters gives much valuable information in relation to abnormalities in the ureters and in their mode of insertion in the pelvis, as well as indicating abnormali-ties in the shape or position of the kidney. In addition, plain roentgenog-raphy gives other valuable information for diagnosis; the kidney shadows in the plain X-ray film may give the first hint of the presence of an ectopic kidney or fused kidney, especially of the horseshoe type. It may show calcified cysts or calculi lying in abnormal positions indicating renal fusion. Sometimes a coraliform stone, the image of which outlines an abnormal type of pelvis or calices, indicates the presence of a malformation of these structures.

Pyelography or urography is the method of examination on which the main dependence must be placed for correct diagnosis of anomalies of the urinary tract. This method, developed in recent years, makes possible the delineation and visualization of the entire urinary tract. There are now two methods of pyelography in use: (1) instrumental, or retrograde, or ascending pyelography, obtained by the injection of an opaque sub-stance through the ureters, and (2) intravenous, or descending, pyelog-raphy, or the injection into a vein of a special type of opaque substance (iopax), which is selected in its effect on the kidney shadow. Descending pyelography may also be obtained by oral, rectal or subcutaneous adminis-tration of the opaque substance. Although this descending method does not give such clear shadows as the ascending method, it is never-theless of great value in cases in which ureteral catheterization is impossible owing to obstruction or anomaly of the ureter. For instance, in aplastic kidney when the ureter is rudimentary and not patent the aplastic mass of renal tissue is shown in the intravenous pyelogram whenever a rudi-mentary artery is present. However, in certain instances when the kidney parenchyma has been entirely destroyed by any pathologic process and there is therefore no kidney secretion, there will be no elimination of the opaque substance and it is necessary to resort to cystoscopy, ureteral catheterization and retrograde pyelography in order to obtain the proper diagnosis. In the diagnosis of renal and ureteral anomalies, when retro-grade pyelography is used, it must be emphasized that a bilateral pyelo-gram is necessary to show the conditions present in the entire urinary tract.

THE HORSESHOE KIDNEY PYELOGRAPHIC TRIANGLE

In the diagnosis of horseshoe kidney, the use of the bilateral pyelogram is essential, as only by this means can the pathognomonic horseshoe kidney triangle be demonstrated (fig. 4). In this type of fused kidney

the calices are in reverse position, directed inward toward the spinal column, bringing the lower calices of the two sides in close approximation to each other, producing a pyelographic picture so characteristic that I have projected from it a triangle—the pyelographic triangle of the horseshoe kidney—with a narrow basal angle, usually less than 20 degrees; in contrast with this the corresponding angle of the pyelographic triangle of the normally placed kidney is between 64 and 90 degrees. This pathognomonic pyelographic triangle of the horseshoe kidney, which I have
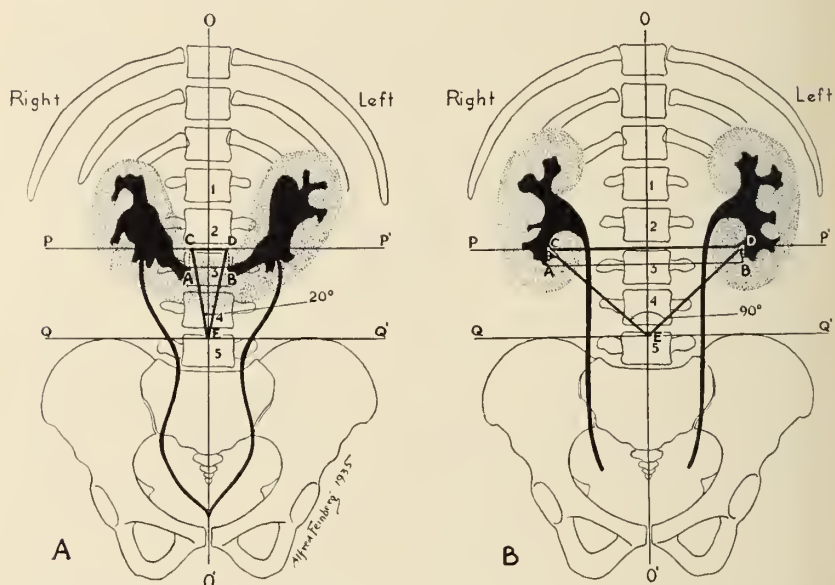
FIG. 4. Diagrammatic drawings of the pyelographic triangle. A, bilateral pyeloureterogram of a typical horseshoe kidney, showing the pathognomonic horseshoe kidney pyelographic triangle with its minimum basal angle of 20 degrees. B, normal bilateral pyelogram showing the normal pyelographic triangle CED with the basal angle at E measuring 90 degrees, the average measurement in 100 bilateral pyelograms of normally placed kidneys. (From Gutierrez, Robert: The Clinical Management of Horseshoe Kidney, New York, Paul B. Hoeber, Inc., 1934.)

described elsewhere, I have found to be of the greatest value in the diagnosis of this anomaly. Other manifestations in the pyelogram of the horseshoe kidney that are of diagnostic value are the possible delineation of the isthmus, the shadow of calculi within the kidney close to the vertebral column or overlapping it, the "flower vase" position of the ureters, and the "bottle neck" shape at the ureteropelvic junction. But of all these the pyelographic triangle of the horseshoe kidney is the most important (fig. 4A).

TREATMENT

In anomalies of the upper urinary tract the treatment to be adopted depends not only on the type of anomaly but also on the presence of any associated pathologic condition. If the anomaly causes no symptoms but has been discovered accidentally, no treatment at all is indicated, as some persons with congenital malformations live indefinitely without developing any clinical symptoms. Such patients should, however, be kept under observation. In some cases only general medical treatment and urologic treatment to secure drainage and relief of infection are indicated. The urologic treatment in these cases includes cystoscopic treatment with lavage of the renal pelvis and the use of indwelling catheters. When surgery is indicated this does not necessarily imply a radical operation. In some cases of hypoplastic and aplastic kidney it is best to remove the infantile or rudimentary organ entirely, provided the remaining kidney has been found to have adequate function. In single kidney only the most conservative surgical measures can be employed in the event of pathologic conditions arising in such a single kidney. In the treatment of cystic or polycystic kidney conservative measures have also been devised, but if only one kidney is involved and the other kidney has normal or nearly normal function, nephrectomy is often the method of choice. In unilateral ectopic kidney when there is an associated pathologic condition (fig. 5 C and D), such as calculus, infected hydronephrosis or tumor or tuberculosis, nephrectomy by the transperitoneal route is always the procedure of choice, provided the kidney of the opposite side has adequate function. In the treatment of hydronephrosis numerous plastic operations on the pelvis and for the derivation of the urine and drainage of the hydronephrotic sac have been used. The conservative operation for hydronephrosis most widely advocated today is the resection of the renal pelvis with complete preservation of the renal blood supply; this type of operation preserves the integrity of the ureter and brings it into a nearly vertical position, which maintains efficient drainage. In some cases of hydronephrosis, however, in which the renal parenchyma has been completely or almost completely destroyed and the kidney rendered functionless, nephrectomy is the operation of choice, always with consideration of the function of the opposite kidney. In some cases with complicating infection and pyohydronephrosis a preliminary nephrostomy, followed by a secondary nephrectomy, is indicated. Where a marked dilatation of the ureter (hydro-ureter) is associated with hydronephrosis, removal of both kidney and ureter is necessary by a combined ureteronephrectomy, as I have described elsewhere. Also this combined procedure can be successfully used in cases of an ectopic ureter in which the kidney and ureter have lost their entire function, and in cases of double kidney and double

ureter in which one is in ectopia, opening extravesically, when a combined ureteroheminephrectomy also is indicated.

In horseshoe kidney disease the ideal treatment is the division of the isthmus, or symphysiotomy, followed by nephropexy or suspension of
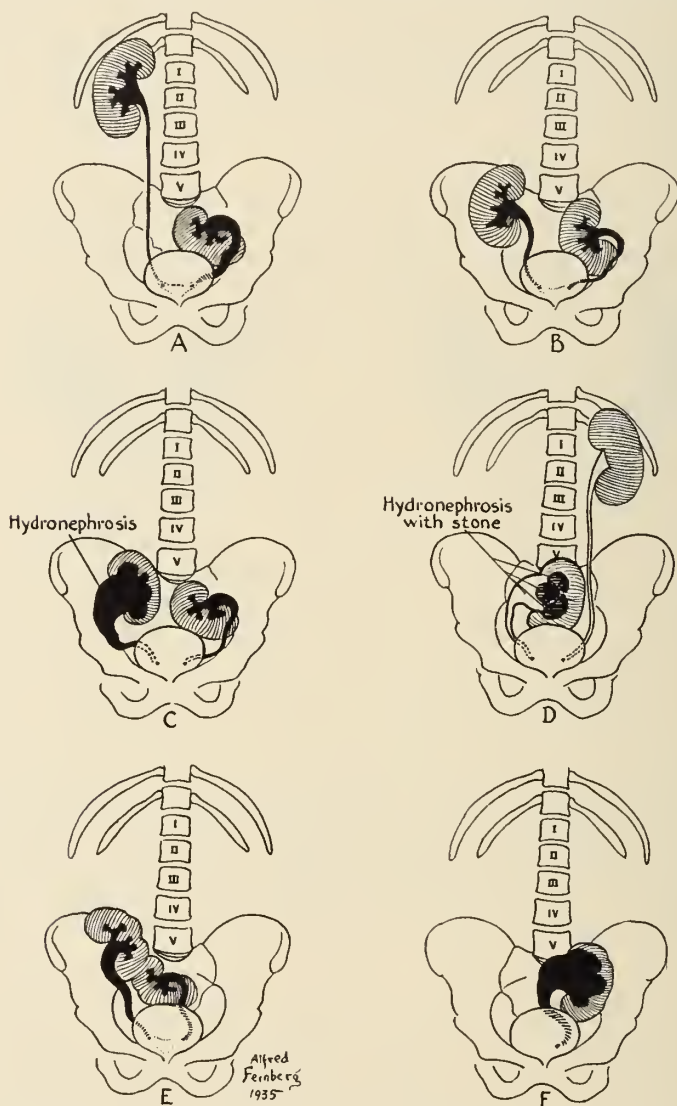
Fig. 5. Different types of unilateral or bilateral ectopic kidney with or without fusion and their surgical treatment when associated pathologic conditions are present, as in C and D, and transperitoneal nephrectomy is indicated: A, unilateral ectopic kidney; B, bilateral ectopic kidney; C, bilateral ectopic kidney with hydronephrosis on one side; D, nephrolithiasis with hydronephrosis in a unilateral ectopic kidney; E, a fused kidney in crossed dystopia; F, a single kidney in ectopia.

one-half of the organ. In this operation the ureters and pelves should also be freed from any bands of adhesions and aberrant blood vessels, so commonly present in association with this anomaly. If there are pathologic conditions involving a half of the organ, any conservative operation can be done, as in the ordinary type of kidney. If one-half of the organ is the site of a pathologic condition that has practically destroyed its parenchyma and rendered it functionless, this half may be removed—a heminephrectomy—provided the remaining half has adequate function. All these operations on a horseshoe kidney should always be done extraperitoneally by the lumbar route of approach in order to avoid peritoneal complications.

REPORT OF CASES

The following three cases illustrate various types of anomalies that caused marked urinary obstruction and confusing symptoms, which required complete urologic and urographic examination for diagnosis and operative treatment:

Case 1. A boy, H. R., aged 2 years, born with an imperforate anus, had been suffering from chronic "pyelitis" and "nephritis" and gastro-intestinal upsets; he had always been a delicate child. He was admitted to the hospital July 8, 1922, with convulsions and a temperature up to 103°F. and died in uremia July 11. Autopsy showed the presence of a well developed glans penis with a double urethra, one opening normally into the bladder and the other being a blind channel. Examination of the bladder, ureters and kidney showed the "golf hole" type of ureteral orifices (fig. 6), with enormous hydro-ureters and hydronephrosis and partial destruction of the kidney parenchyma, more marked on the left side; also bilateral pyelitis and pyelonephritis; this obviously resulted in actual destruction of kidney function, which was the direct cause of death.

Comment. This case shows the concomitant occurrence of congenital malformations of the upper and lower urinary tract, as well as abnormalities of the intestinal canal. Cases of this kind demand a complete urologic and urographic examination and early surgical treatment in order to relieve the surgical condition.

Case 2. A woman, aged 48, had been suffering from occasional lumbar pain and gastro-intestinal disorders since childhood. She had been repeatedly examined in the past twenty-five years for the gastric symptoms and pain in the left upper quadrant. She had also had occasional urinary disturbances with frequency of urination, a slight dysuria and microscopic pyuria and hematuria. She had diabetes and had been treated by diet and insulin. For the past five months she had noted shortness of breath and fatigue on slight exertion and had complained of menstrual irregularities. She was given a gynecologic examination by Dr. David Barrows at

the Hospital for the Ruptured and Crippled, who diagnosed a calcified cyst of the right ovary and, in view of her bladder symptoms, referred her to me for urologic examination. July 16, 1934, on cystoscopic examination, I found multiple flecks of pus at the fundus of the bladder, and a normal ureteral orifice on the right side, which was readily catheterized. On the left side the ureteral orifice was very small and of a pin-point type and could not be catheterized with a No. 6 French catheter; but after the
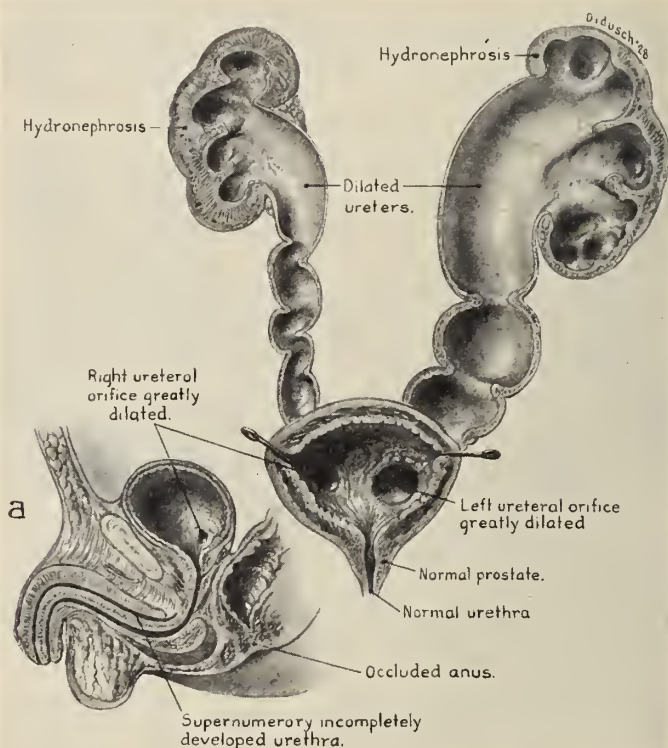
FIG. 6. Drawing from post mortem specimen showing congenital "golf hole" type of ureteral orifice, causing hydro-ureter and hydronephrosis, in a boy 2 years old, with double urethra and occluded anus. Erroneously diagnosed as chronic "pyelitis" and "nephritis"; the patient died in acute uremia from renal failure.

passage of a No. 4 bougie it admitted a No. 5 French catheter, although with difficulty and definite obstruction. The phenolsulfonphthalein test showed normal function of the right kidney but no excretion of the dye in twenty minutes on the left side. The plain roentgenogram revealed the calcified cyst of the right ovary. The retrograde bilateral ureteropyelogram showed a normal kidney and ureter on the right side and an enormous hydro-ureter and hydronephrosis on the left side (fig. 7). The

latter was removed by a combined total ureteronephrectomy by my technic, described elsewhere. The patient had an uneventful recovery, leaving the hospital in three weeks; she is now free from symptoms, nine months after operation.

Comment. This case illustrates the value of a complete urologic examination in an effort to establish an accurate diagnosis in doubtful cases with abdominal symptoms of long standing that may be due to congenital malformations of the urinary tract. It also illustrates that, in cases of hydro-ureter and hydronephrosis, when the diagnosis has been urographically made before the operation, the two-stage surgical procedure of combined ureteronephrectomy has its proper indication. At the same

Fig. 7. Congenital stricture of the intravesical portion of the left ureter, causing hydro-ureter and hydronephrosis. Cured by combined total ureteronephrectomy.

A. Bilateral pyeloureterogram showing the enormous hydro-ureter and functionless hydronephrosis on the left side.

B. Ureteropyelogram of the specimen removed in toto by the author's method of combined ureteronephrectomy.

C. Drawing of the same specimen showing the enormous size of the hydro-ureter and of the congenital hydronephrotic kidney.

time, when the diagnosis is not actually made before the operation, and the pathology of the ureter is not properly recognized in advance, it goes without saying that nephroureterectomy, as carried out by Beer, may be the best operative choice in some of these cases. But, either way, the fundamental principle stands firm that the ureter must be removed in toto with the kidney whenever an associated pathologic lesion of the latter is present.

Case 3. M. G., a woman, aged 40, complained of intermittent attacks of retention of urine with dysuria, frequency, burning and difficulty in urination. Cystoscopic examination revealed two pedunculated mobile masses in the bladder; the one at the right side was so large that it covered the beak of the cystoscope. The first impression was that of a large tumor

of the bladder. Further inspection of the left ureteral orifice during ejaculation of urine revealed the presence of a small ureterocele, and it was then discovered that a large pedunculate mass on the right side was also a ureterocele (fig. 8). As both ureteral orifices were of the pin-point
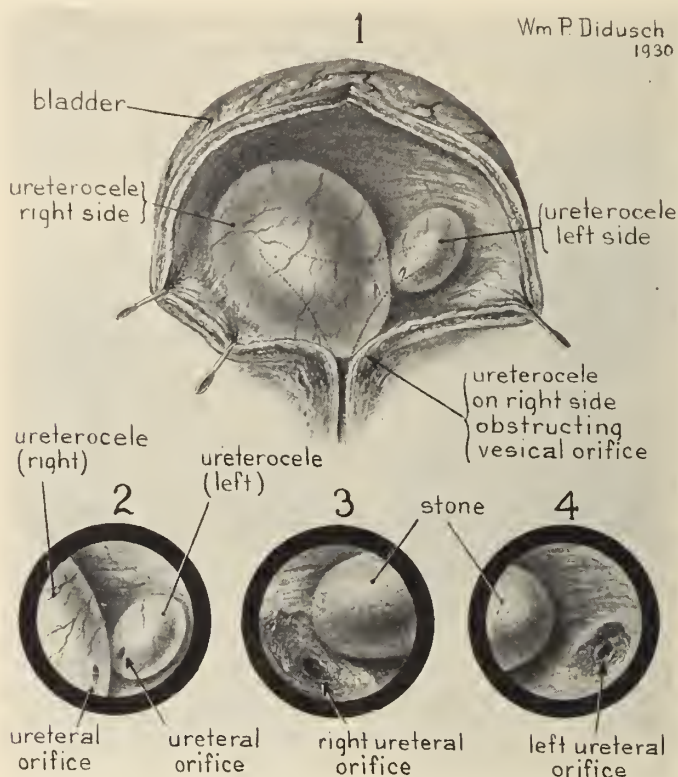
FIG. 8. A. Bilateral ureterocele causing complete retention of urine in a female with duplication of the ureters and kidney pelves.

(1) Cystoscopic view of the bladder showing the actual size of the two ureteroceles producing mechanical obstruction at the vesical orifice.

(2) Cystoscopic view showing the two congenitally strictured ureteral orifices during ejaculation.

(3 and 4) Cystoscopic view of the right and left ureteral orifices three weeks after fulguration and ureterotomy showing the sloughing tissue around the newly opened ureteral orifices. The stone which was in the ureterocele and which was removed by cystoscopic manipulation, can now be seen in the bladder after fulguration.

type and could not be catheterized, it was decided to fulgurate both orifices through the cystoscope in an effort to destroy the ureteroceles and create new ureteral orifices. This was successfully accomplished, and three weeks later when the patient returned for further treatment the cystoscopic examination revealed a good-sized stone about the size of a

pigeon egg, which came from the larger ureterocele and which was readily seen in the fundus of the bladder. This stone was crushed with the cystoscopic rongeur and entirely removed by further manipulation. At a later date both ureters were catheterized with ease and a retrograde bilateral ureteropyelogram was made, revealing a congenital malformation of the upper urinary tract—reduplication of ureters and renal pelves on both sides with a slight pyelitis and hydronephrosis. On account of the presence of this infection, a course of cystoscopic treatments was given, with dilatation of the ureters and lavage of the renal pelves. This promptly relieved the symptoms and there has been no recurrence to date.

Fɪɢ. 8B. Bilateral ureterocele causing complete retention of urine in a female with duplication of the ureters and kidney pelves.

(5) Bilateral pyelo-ureterogram made after the fulguration of the ureterocele, showing the duplication of the ureters and kidney pelves on both sides.

(6) Drawing from the bilateral pyelo-ureterogram showing graphically the concomitant anomalies which can only be discovered by routine urologic and urographic examination.

Comment. This case illustrates the important rôle played by anomalies of ureters and kidneys in diseases and surgical conditions in the upper urinary tract, which can be cleared up only by proper urologic and surgical treatment. It, therefore, reveals the importance of routine cystoscopic examination and the value of high frequency fulguration for relief of the ureterocele—a method which has been so brilliantly introduced by Edwin Beer for conservative treatment of tumors of the bladder, and which has its best application in this type of pathologic condition.

SUMMARY AND CONCLUSIONS

My purpose in this article is to present a brief review of the congenital anomalies of the kidney and ureter and to call attention to the frequent occurrence of associated pathologic conditions that cause clinical symptoms

and require surgical treatment. The classification presented shows the numerous anatomic varieties of these anomalies and also indicates the clinical and pathologic conditions associated with such anomalies.

The clinical syndrome and the pathognomonic diagnostic sign of horseshoe kidney disease illustrate the clinical importance of congenital abnormalities of the urinary tract.

The conclusions to be drawn from this presentation and to be emphasized are the importance of complete urological and urographic examination in every case in which there are obscure abdominal symptoms and minor urinary symptoms, and the excellent results that can be obtained by proper surgical methods when a correct diagnosis is thus established.

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VESICAL MUSCULAR ATONY

Illustrated by a Case Following Suprapubic Prostatectomy

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The first meeting of the International Urological Society was held in Paris in 1905, under the presidency of Guyon. Dr. Samuel Alexander entered into the discussion of 'Retention of Urine without Prostatic Enlargement'. Previous speakers had debated the then mysterious subject of *prostatisme sans prostate* but he elected to introduce a more physiological note; he spoke of the retention of urine that occurs in typhoid fever in the absence of urethral or prostatic obstruction and distinguished the bladder weakness due to (1) toxic muscular atony, that due to (2) mucosal anesthesia from the typhoid state and that due to (3) inattention or stupor.

At the time the contribution seemed to me a pretty one, but only distantly related to the problems of the urologist. But in the last ten years I have been impressed by the fact that the combination of muscle weakness, mucosal anesthesia and inattention is one we have always with us. It is perhaps most often encountered in the form of postoperative retention of urine. Such, also, is the retention of urine in hysteria, in the insane and in the aged.

Sir Henry Thompson believed that after three years of chronic retention of urine behind an obstructing prostate the bladder becomes so weak that it cannot be expected to resume efficient function, however fully the obstructing prostate is removed. A urological generation followed him in this, till Fuller taught us the truth, that no degree of muscular weakness incapacitates the bladder completely.

Yet every prostatic we operate upon, by whatever method, is likely to regain his capacity to empty the organ completely only after a number of attempts at urination, perhaps only after a few days. We are accustomed, I think, to attribute the loss of function to slight persistent obstruction, the result of mucosal swelling, etc. I wonder whether many of the cases are not rather examples of postoperative retention in an aged, tired bladder. The following case is an extreme example of this.

E. M. S., was 78 years old, unmarried and sexually inactive, when he consulted Dr. McLellan for the relief of an acute and all but complete retention of urine of three days' duration.

The patient's forbears had died young; he had a brother from whom I had

removed a very large hypertrophy of the prostate some eight years before and who, though still alive, is senile at the age of 81.

The previous personal history is irrelevant, until at the age of 68 he consulted me for urethrorrhagia due to a spontaneous urethral ulceration near the bulbomembranous junction (such as has been described by Hurry Fenwick). This was relieved by a few dilatations.

In 1935, his 77th year, he required drainage of the left eye for glaucoma and submitted to a general physical examination in preparation for this. The prostate was much enlarged by rectal touch, with deep central sulcus. There was a constant retention of about 100 c.c. of uninfected urine. A brief course of irradiation was administered to the prostate and his slight nocturia was thus relieved.

The eye was operated upon and within twenty-four hours he became actively delirious; the bandage had to be removed from the good eye but, even so, his delirium abated slowly and entire mental clarity did not return for several weeks. There was no suggestion of retention of urine during this period.

The nocturia reappeared eighteen months later but was of no moment until December 1936. Then he caught a bad cold and, while convalescing from this, walked seven miles one day, this being his normal daily round when well. This was the day after Christmas. On the 31st, he consulted Dr. McLellan.

He looked toxic, was distinctly incoherent, his bladder above the umbilicus. He was promptly sent to the hospital for decompression. On admission the blood showed 12,000 leucocytes and 28 mgm. of urea nitrogen. The bladder was emptied after two days' decompression. 'Phthalein excretion was then 65 per cent in two hours after intravenous injection. Cystourethrogram showed large prostatic intrusion and several bladder stones. There were many hemorrhoids and a few râles at the bases of the lungs. X-ray examination showed extensive healed pulmonary tuberculosis, of which he gave a history in his twenties. There was middle ear deafness; the glaucoma was controlled.

Under decompression he became more delirious. Fluids were forced and on the fifth day vasotomy and suprapubic drainage were performed. His mental condition then began to improve; at the present time he does not remember any of the events that preceded the prostatectomy, though he does remember that operation. It was performed by Dr. McLellan two weeks after the suprapubic drainage.

Convalescence was uneventful but for a severe secondary hemorrhage on the sixth day. This was controlled by Pilcher bag and blood transfusion. The suprapubic fistula healed on the twenty-fourth day. At this time his mental equilibrium was by no means established. He did not know January from July and, though a lawyer and an accountant

of sorts, could neither copy a column of figures nor add them up. His operations were in January, his income tax report was completed in May.

Imagine our consternation, therefore, dealing with this unhinged patient, to find that when the fistula healed he could not urinate a drop. His patient bladder was emptied three times a day by catheter for a few days, then only morning and night, in the hope that the distension of his bladder might induce micturition. This hope was not realized, though examination did not reveal any urethral obstruction.

At the end of a week of this, Dr. McLellan was one day urging him to urinate when he appreciated that the patient's vesical atony was partly due to inattention. He had been so long without urinating that, seemingly, he had lost the knack of directing his will to this function. A sharp command brought his mind to attention and evoked a feeble stream that left no more than 100 c.c. of residual urine.

The patient had now been almost two months in the hospital and we were delighted to send him home with a nurse. The record of the first three days thereafter is as follows:

Feb. 27th—	1:00 P.M.	Catheterized	240 c.c.
	10:00 P.M.	Catheterized	330 c.c.
Feb. 28th—	3:00 A.M.	Voided	390 c.c.
	6:00 A.M.	Catheterized	360 c.c.
	6:00 P.M.	Voided	240 c.c.
	8:00 P.M.	Catheterized	270 c.c.
March 1st—	6:00 A.M.	Voided	390 c.c.
	6:15 A.M.	Catheterized	305 c.c.
	7:00 P.M.	Voided	480 c.c.
	7:15 P.M.	Catheterized	90 c.c.
March 2nd—	6:30 A.M.	Voided	600 c.c.
	6:40 P.M.	Catheterized	135 c.c.
	4:00 P.M.	Voided	480 c.c.
	9:00 P.M.	Catheterized	240 c.c.
March 3rd—	6:00 A.M.	Voided	255 c.c.
	6:20 A.M.	Catheterized	390 c.c.

Thus he continued until, on March 12th, the nurse was scolded for not making the patient urinate. Thereafter he was commanded in no uncertain tones to urinate at six hour intervals and the bladder irrigated daily with 1/2000 silver nitrate solution and from that time the residual urine never exceeded 50 c.c. The convalescence was otherwise uneventful except that the urine remained grossly purulent until the patient passed a small stone early in June. A month later he remained well. He holds his urine eight hours at night. It is grossly clear.

COMMENT

In the absence of organic lesion of the nervous system, retention of urine may persist after relief of prostatic retention. This retention may

result from a combination of intellectual apathy (senile or toxic), muscular atony of the bladder and mucosal anesthesia. Such functional atony is a familiar phenomenon after pelvic operations upon women. It occurs so rarely in any marked degree after operation for the relief of prostatic obstruction that its causes are commonly overlooked.

Psychic treatment combined with irritating injections into the bladder are calculated to relieve this condition.

THE PRINCIPLES OF THE SURGERY, HOSPITALIZATION AND THE EVACUATION OF THE WOUNDED IN THE ARGONNE-MEUSE OFFENSIVE*

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The battle casualties of the Great War differed from those of the previous wars in the overwhelming proportion of wounds caused by high explosives. The Germans in the Franco-Prussian War in '71 had 9 per cent of shell wounds and 90 per cent of bullet wounds. The Japanese in the Russian-Japanese War had 8.5 per cent shell wounds and 85 per cent bullet wounds. The average for the French in 1914 was 75 per cent shell wounds and 23 per cent bullet wounds. This average was maintained throughout the War with some variations in the different battles. In open warfare it dropped to 70 per cent shell wounds and 30 per cent bullet wounds. In the A. E. F. the proportion was 2.9 shell wounds to one bullet wound. Bayonet wounds, etc. were twenty-six one hundredths of one per cent of all wounds inflicted.

In order that you may visualize what a storm of steel is like, let us examine the figures for the opening day of the Argonne-Meuse Offensive. The battle began at 11:00 P. M. on September 25, 1918, on a twenty-two kilometer front. There was one gun for every eight meters of front. Five hundred and eight aeroplanes and seventy-three tanks were in action. More than 250,000 rounds of artillery were fired, the caliber of the guns ranging from 75 to 340 mm. To this weight of metal we must add the aeroplane bombs and the innumerable hand and rifle grenades. If we keep this picture in mind, the preponderance of shell wounds in modern warfare is readily understood.

In action the Chief Surgeon of the Army has a threefold mission:

(1) He must provide an efficient evacuation service that will promptly relieve the combatant troops of their sick and wounded, and thus assure to the Commanding General freedom of action;

(2) He must provide a section of hospitalization for their reception and treatment, so organized that as many of the wounded as possible will be returned to duty;

(3) He must promptly clear his hospitals of all cases which can be safely evacuated to the zone of the interior.

* Read before the Ninth Annual Graduate Fortnight of The New York Academy of Medicine, Military Evening, October 22, 1936.

These objectives can only be obtained by the closest coordination between the sections of evacuation and hospitalization.

An efficient evacuation and hospitalization is the backbone of all treatment; without it surgery is hamstrung. The efficient functioning of these services is an essential factor in supporting the morale of the combatant troops. Disregard of this by military authorities has lead to demoralization and, in one notable instance, to mutiny. A prominent commander summed it up as follows: "I would not care to lead any infantry unit into battle more than once if that unit knew that no medical aid was at hand."

Wounds resulting from the explosive action of bullets and those from deformed and ricochetting bullets were treated as shell wounds.

In the First Army there were four methods of treating shell wounds:
(1) Incision, drainage and removal of the foreign bodies;
(2) Primary suture of the wound;
(3) Delayed primary suture;
(4) The Carrel method.

Experience has shown that the primary suture of wounds, in the hands of trained men, gives the most brilliant results and this often in places where you would least expect it, as, for example, in the joints and in the chest. The method calls for good judgment, the early reception and the retention of the patient under the care of the operator for a period long enough to insure that the wound is progressing favorably.

The primary closure of wounds was taught and practised in the thirteenth century by Theodoric (1205–1298) and Henri de Mondeville (1260–1320). They advised a wide incision, the removal of all foreign bodies and the freshening of all wounds that had been exposed, this to be followed by a primary closure. Baron Larrey, who practised débridement and primary closure during the Napoleonic wars, credits Desault with the origin of this method. The honor of employing primary suture in the Great War justly belongs to Colonel Grey of Aberdeen (now Montreal), the consultant to the British Expeditionary Forces, at Rouen, November, 1914. This was the first great surgical contribution of the War.

Primary suture is indicated in fresh wounds that are less than twenty-four hours old, and if the military situation is such that the patient can be retained under the control of the operator. The first step is débridement. This completed, and a careful hemostasis established, the wound is sutured, an aseptic dressing applied and the part immobilized. It is contraindicated in all wounds over twenty-four hours, and where the patient's general condition is low from shock, hemorrhage or exposure. Here the pulse is a better guide than the temperature. A pulse rate of 110 to 120 precludes primary suture. It is contraindicated in areas where the arterial supply has been damaged, in massive infiltrating hematomas, in the presence of Lemaître's sign, in dry vascular wounds, in deep lesions

with extensive destruction of tissues, and also where the surfaces of the wounds have a grayish, brownish green or pulpy appearance. Judgment is required in the presence of multiple wounds.

Delayed primary suture can be performed on fresh wounds twenty-four to thirty-six hours old. The first step is débridement, the second, suture. If the patient cannot be retained in the same formation, or if gas gangrene is suspected, the suturing should be omitted. Although the ideal time of suture is from the third to the sixth day, it can be practised as late as the tenth or twelfth day. This method was not employed in our Army to the extent that it deserved. It gives good results, has a wide application, and is less dangerous than primary suture.

The Carrel method consists of a mechanical and a chemical sterilization plus a secondary suture under bacterial control. The first step is a thorough débridement; the second is the introduction of the instillation tubes. It must be clearly understood that the Carrel method is not a continuous irrigation. It is a mechanical attempt to deliver an antiseptic of definite chemical concentration (sodium hypochlorite 0.5 per cent) to every portion of a surgically prepared wound and to insure a constant contact for the desired period. The final step is the suture of the wound. This is undertaken when three successive bacterial counts taken on alternate days show the wound to be free from bacteria. Wounds of the soft parts are sterilized in from five to eight days; extensively traumatized wounds take longer; fractures from two to four weeks. The method is safe, it gives excellent results, has the widest application and in the infected wounds it has proved to be superior to the other methods. This was the second great contribution to military surgery.

Débridement is the basic principle underlying the methods of primary suture, delayed primary suture and the Carrel method. The success or failure of any one of these methods depends directly on the thoroughness and gentleness with which the procedure is carried out. The successful débridement of certain types of wounds calls for experience, judgment and skill. Long deep muscular wounds involving important structures, wounds of joints and wounds of the chest should not be entrusted to the novice.

Débridement should be preceded, where possible, by an X-ray localization. It consists of thorough, methodical, mechanical disinfection of the wound with the extraction of all shell fragments, particles of clothing, dirt, etc. The field of operation is painted with the tincture of iodine. The bruised and necrotic edges are trimmed away with a sharp knife. The delimiting skin incision should be elliptical in type and correspond to the axis of the limb. The knife and forceps are laid aside and new instruments are taken. From this stage the manner of debridement will vary according to the type of the wound.

The Débridement of Gutter, Penetrating and Perforating Wounds. Gutter

wounds should be laid open like a book and gently explored for shell fragments, pieces of clothing, pockets, etc.   Everything that could have been infected or could become the source of infection is removed, all non-infected tissues unlikely to become infected are preserved.   Gentleness of manipulation and thoroughness are the keystone of the technic. Brutalization of the traumatized tissue is a technical crime.

Penetrating and perforating wounds, if superficial, can be converted into gutter wounds.   If the wound is deep, another technic is employed to excise the tract.   The skin surrounding the orifices of the wound is treated as in the gutter wounds.   If the ellipse of the skin incision has been laid parallel to the axis of the tract and more room is needed, extensions can be made in the desired direction.   The underlying fascia is excised around the entrance of shell fragment.   The edges of the orifice are lifted up by clamps in order to see where the tract in the muscle goes.   Incise the fascia and adjacent muscle to expose the tract.   Under sight with a curved scissors the portions of muscular walls which are abnormally colored or which fail to bleed or contract are excised.   All foreign bodies— dirt, particles of clothing, etc.—are removed, retractors are inserted, and the next segment is treated in the same way until the shell fragment is found and removed.   In a perforating wound of an extremity the excision should begin at the orifice of the wound which shows the least damage; excise the tract as far as you can, pack the cleansed tract with gauze and excise from the other wound opening till the gauze packing is exposed.

In a penetrating wound where the shell fragment is near the opposite surface from that of the wound of entrance it may be more easily removed through a direct excision over it; the wound tract to be excised as above. If you lose the tract do not depend on probing, as nine chances out of ten the probe will make a false passage.   Get a good exposure, with good hemostasis.   Examine all clots, portions of clothing, ecchymotic spots, pockets, etc., and you will rediscover the lost tract.   Do not forget that the tract between mobile muscles or tendons may be only covered up; flex and extend the limb and you may uncover it.   Remember that the spaces between the moving muscles often harbor small amounts of clothing. In the long tracts of wounds running parallel to axis of the limb two or three separate incisions may be needed to complete the débridement.

The same minute and careful mechanical cleansing is carried out in osseous wounds and wounds of the joints as in the soft parts.   A conservative attitude toward the removal of bone fragments was the approved practice.   In the early years of the War 80 per cent of the amputations were due to infection.   Débridement, primary suture, the Carrel method and efficient splinting were the factors in cutting down this percentage.

Wounds of the Abdomen.   The English in the South African campaign of 1899 practised systematic surgical intervention and had a mortality

of 95 per cent. Such mortalities lead to a policy of non-intervention. As a matter of fact, in the early months of the Great War the military situation precluded any other policy. However, the mortality from shell wounds was so great that the policy of non-intervention had to be abandoned for that of early systematic surgical intervention. The army evacuation and hospitalization services were reorganized to meet this situation, and a substantial lowering of the mortality was obtained.

Wounds of the Chest. The great predominance of bullet wounds in the former wars had led surgeons to believe that these wounds were relatively benign, the mortality being about 3 per cent. With the increase in the use of artillery, bombs, grenades, etc., the mortality rose sharply. Twenty-five per cent died in the divisional formations, 20 per cent in the Evacuation Hospitals, and of the remaining 55 per cent evacuated to the rear 3 per cent died from complications, a total mortality of 48 per cent. The expectant treatment was dropped and the evacuation and hospitalization so organized that these cases could be promptly operated on. The treatment consisted of an excision of the wound tract, extraction of projectiles, clothes, bone fragments, etc., with air-tight closing of the wound and aspiration of the air. As pneumothorax and infection were considered to be the dangerous factors, all sucking wounds, if they could not be closed temporarily by simple suture, were sealed with an air-tight dressing and tightly bandaged to the chest until they could be operated upon. The gratifying results obtained in this difficult field was one of the brightest spots in the surgery of the War. The lessons learned and the experience gained have done much to advance the thoracic surgery of civil life.

Wounds of the Cranium. In the early months of the War the French had a mortality of 15 per cent. After the adoption of the steel helmets it dropped to 12 per cent. At the same time the percentage of the minor wounds rose, showing that the helmets did much to protect the soldiers' heads from shell and grenade fragments.

Wounds of the cranium are safely transportable before operation and non-transportable after operation. They can be classed as wounds of secondary urgency as contrasted to the chest and abdominal wounds, which are of first urgency. The ideal place for the treatment of these cases is an evacuation hospital center where skilled help can be obtained and the retention of the patient assured for a reasonable length of time.

Wounds of the Nerves. A simple uncomplicated division of the nerve calls for primary suture. Complicated wounds with loss of substance or associated with fracture or vascular lesions, etc., should be treated by débridement, correctly splinted and then evacuated to the interior. It is sometimes very difficult to make a diagnosis between contusion and severance of the nerve. If in doubt, the expectant treatment can be tried. No matter what the lesion is, all involved members must be splinted in

the position of physiological balance. The immediate diagnosis is rendered difficult in associated vascular lesions where the tourniquet has been abused.

Vascular Lesions. The treatment is that of civil life. The following conditions are rare in civil life; massive hemorrhages into the tissues which, if unrecognized and unchecked, may cause death; large infiltrating hematomas causing pressure necrosis and gangrene of the extremity; dry vascular wounds (Plaies Vasculares Séches). The latter term is applied to wounds in which the vessels are injured, but there is no hemorrhage from the wound, no hematoma, no diffuse infiltration. This phenomenon is caused by the contraction of the coats of the severed vessel and the presence of a clot, clothing or shell fragment plugging the vessel. The clinical interest lies in the fact that when the blood pressure rises severe secondary hemorrhage can occur. The treatment of these dry vascular wounds consists in the search for and ligation of the damaged and plugged vessels.

Evacuation. The sick and wounded were brought to the Army hospitals by ambulances, trucks, sight-seeing buses, and by the 60 cm. and 1 metre railways. From the railhead hospitals they were evacuated to the S. O. S. by French and American Hospital trains.

The Evacuation by Motor Transport. On a proper triage an adequate mobile motor transportation, and the will to see it through, rests the success of the evacuation of the wounded.

The character of the terrain, the great number of troops to be employed in this offensive, coupled with the scarcity of ambulances, made it self-evident that the measures used in the Chateau-Thierry and St. Mihiel offensive would be entirely inadequate to meet the probable strain. On assuming command of the ambulances September 20, 1918, there were only ninety-three available ambulances. The C. S., recognizing the imperative need for more ambulances through G-4, had the whole Army combed for cars. On the morning of September 26th four hundred ambulances, sixty trucks and thirty sight-seeing buses had been assembled. The bed capacity of the Army hospitals was eighteen thousand; the number of men in the Army, over one million. Judged by the tables of organization we lacked three hundred and fifty cars. Faced by such a shortage it was vital that plans be devised to keep every wheel moving. In order to make the First Army's medical transportation liquid all trucks, ambulances, motor cars, motor cycles, etc., were pooled and placed under the control of the Ambulance Director.

The shortage of division and corps ambulances was considered a preferred need, and the Army strained every nerve to make this shortage good. This was accomplished by the temporary loaning of extra ambulance sections to the Corps, who in turn assigned them to Divisions while these Divisions were in action. By this plan, instead of being tied

down to a Division, the ambulances were controlled by the Army through the Corps; and when an emergency arose they were readily shifted to the point of greatest stress. As an example of the inadequate ambulance transportation with which some of the Divisions entered the Army, one Division in the First Corps arrived at the last moment for combat with four Fords and eight G. M. C. ambulances. Another Division came in with a carrying capacity of less than thirty-two patients. The poor Pioneer regiments had no ambulances at all.

The Plan of the Disposition of Ambulances for the Offensive of September 26, 1918, in Relation to Army Hospitals. The wounded were evacuated from the battle line to the field hospitals by the divisional ambulance companies,—from the field hospitals to the evacuation hospitals and special hospitals by the corps ambulances. The Army furnished extra ambulance sections and ten sight-seeing autos in addition to the ambulance sections already furnished to the corps. In return the corps took care of any Army troops requiring evacuation in their respective areas. The Army provided for the evacuation of the special, mobile, gas and evacuation hospitals.

The Technic of the Evacuation of the Army Hospital. The decision to evacuate was determined by a combination of three factors: the number of empty beds at the Army's disposal, the number of evacuable cases, and the possibilities regarding the reception of wounded in the next twelve hours. The hospitals that were situated at the railhead loaded directly on the trains, while the cases from the outlying hospitals were collected and brought to the railhead by the Army ambulances. Here they were housed in evacuation section until the arrival of the train. The handling and storage of cases from the outlying hospitals during the rush period proved to be a pressing problem. There were over seven thousand active beds at distances of from nine to thirty-five kilometers from the railheads. The care of these cases was one of the weakest points of our evacuation hospitals, due in large measure to the fact that the Commanding Officers of some of the railhead hospitals did not grasp in the earlier part of the offensive the true function of railhead hospitals. One of the essential functions of such a hospital was an efficient evacuation department to handle just such a situation. There was a great tendency, and naturally so, to expand and elaborate the section of hospitalization to the detriment and neglect of the section of evacuation. It is clearly the duty of the railhead hospital to expedite the clearance of the outlying hospitals by every possible means and not to regard such cases as impositions foisted on them, or to resent it as a fancied attempt on the part of another Commanding Officer to "put it over them."

Handling of Lightly Wounded in the Army Hospitals, And Its Relation to the Army Evacuation Service. The evacuation service and advising surgical service of the Army felt keenly that entirely too many unoperated cases were being evacuated. In the first phase of the Offensive 11,370

cases were sent to the rear for operation. Every one of these 11,370 supposedly simple cases were potential sources of trouble through the possibility of their wounds becoming infected. Reports from the rear soon showed that our fears were well grounded. Every effort was made by the Chief Surgeon to correct this glaring error. A study of the situation showed that the failure to produce a greater operative output was due to the failure of the hospitals to provide an efficient plan of triage and treatment of the lightly wounded. This was due to the inexperience of many of the teams in this new field of work, and to the inherent difficulty of making professional men think of the wounded in terms of military values rather than in terms of professional interest. Most of the hospitals seemed to be satisfied with an average of one case an hour per table. Many of the teams came into the Army area with this erroneous notion. Due to the efforts of Lieutenant Colonel Clinton, of the Chief Surgeon's office, and Major George Davis, the fallacy of the idea was exposed, with the result that radical changes in the handling of the lightly wounded were instituted. The lightly wounded were retriaged, assigned special X-ray equipment, special operating rooms and teams specially trained in this type of case. Experienced men of good judgment, who thought and acted quickly, were chosen for this work. The slow, careful operators were assigned to other types of cases. All these special teams were given opportunities to observe the system employed by Majors Davis and Sherbondy. The pioneer team headed by Major Davis actually cleared over ninety cases in several of their shifts; the second, headed by Major Sherbondy, cleared eighty—and it was not long before many of the teams reached an average of sixty. The great practical value of these changes were seen in the fact that in the second phase of the Offensive only 293 unoperative cases were evacuated. This shows what energy, organization and determination can accomplish in the face of a seemingly hopeless proposition. The English Casualty Clearing Stations considered their maximum operative output to be 50 per cent of the wounded received. The credit of this feat is largely due to the foresight, interest and loyal support furnished to the professional and evacuating services by the late Colonel Alexander Stark, Chief Surgeon.

The medical personnel of the First Army can justly feel proud of this splendid achievement. The writer knows of no other result of our own Army or the Armies of the Allies that can match it.

Special Surgical Hospitals in the Army Zone in Relation to the Evacuation Service. In the war of position it had been thought advisable to establish special hospitals in the advanced areas. Due to the determined advocacy of some enthusiasts a tentative trial of a special hospital was made. The impracticability of triaging selected cases, and the fact that the proper functioning of these hospitals necessitated a separate transportation service with its consequent waste of valuable ambulances, soon convinced

the most ardent advocates that this plan was a failure both from the military and the professional standpoint. The original plan as laid down by the Chief Surgeon of having special operating teams stationed at the evacuation hospitals to handle cases that required unusual technical experience was continued.

Professional Care of the Wounded in Relation to the Evacuation Service. Liason between the professional service and the evacuation service was facilitated by the fact that the Director of Ambulances and the Evacuation of Wounded was, in addition, the Chief Consulting Surgeon of the First Army. The Consultants endeavored to bring into the office of the Chief Surgeon information that would be of value to him in the improvement of the professional care of the wounded, and at the same time to furnish him with the detailed information regarding the proper care of the patient in the Divisional and Corps areas. The objects sought by the Chief Surgeon were the better general control of the professional care of the surgical patients, the improvement in the product of the Army hospitals, and a decrease in the number of pre-operative cases evacuated from the area. Each hospital was informed that its surgical rating would be judged not by the number of cases passed through it, but by the number of cases completely operated upon. They were made to understand that to send out unnecessarily pre-operative cases was a mark of military inefficiency and would be so judged.

The reports showed that there was considerable difference in the evacuating time of the divisions. That is, the time that elapsed between the wounding of the patient and his reception in the Army hospitals. The reports from the Army hospitals showed that the best results in cutting down infection and saving life were obtained by those divisions which, in spite of all difficulties, managed to get their cases back in good time. The marked difference between some of the divisions was due to the fact that there was a tendency in certain of them to hold the cases for operation. The condition of the roads failed to explain the marked discrepancy between the divisions. There were certain divisions which, from the moment they entered the Army area till they left, managed to get their cases back promptly.

Influenza in Relation to the Army Ambulance Service. At the staff conference October 17th General Ludendorff made the following statement "At the front the enemy's attacks of yesterday have not succeeded. The enemy did not come on with his usual ardor. If he had done everything he could we should have been beaten. At these points the fighting power of the Entente has not been up to its previous level. Further, the Americans are suffering severely from influenza." The suddenness of that memorable wave of influenza which swept over the Army will never be forgotten by those who served in the Army Ambulance Service. Days and nights of anxiety followed one another in rapid succession. The

wounded were pouring in, the number of sick was mounting, and an exhausted ambulance personnel was being rapidly depleted. Each man was made to feel the seriousness of the crisis we were facing. To have failed at this point would have decidedly embarrassed the military operations.

The personnel of the A. A. S. sprang into the gap and kept every wheel turning, some of the commands performing four times their work with one half of their personnel. No greater personal sacrifice was made anywhere than by these men. Besides transporting the wounded they handled 30,000 sick within a very short period of time.

Personnel of A. A. S. The remarkable spirit shown by the officers and men of the A. A. S. during the Argonne-Meuse Offensive was the finest tribute to those who organized and trained these men in America. No task was too hard for them, no sacrifice too great, no discouragement could dampen their ardor. Continued rains, mud, fatigue, night bombing, blocked roads, etc., meant nothing to them. Youth could not be denied. The constant care and tenderness evinced by the fatigued drivers for their wounded "buddies" was inspiring. The Army ambulance service, with the exception of one section, received no rest or relief during the Argonne-Meuse Offensive. All day and all night a ceaseless stream of ambulances bore their precious freight to the doors of the Army hospitals. "The men on the stretchers were still in their bloody tunics, rain-soaked and in pain, silent, with smashed bodies but undimmed spirits."

The safe arrival of his load of wounded was the ambulance driver's reward. He had forgotten self and served his corps and his country with a devotion equal to that of the wounded soldiers he was carrying. It is with just pride that the officers and men of the evacuation service of the First Army can look back on the work they accomplished. With inadequate personnel and equipment they served an Army of over one million men. They met every difficulty and did their work quietly, swiftly and well; yet many of the units functioned for the first time in this battle.

That their work was appreciated can be seen from the following:

HEADQUARTERS FIRST ARMY
AMERICAN EXPEDITIONARY FORCES
FRANCE

OFFICE OF THE CHIEF OF STAFF

November 7, 1918.

From: Chief of Staff, 1st Army.
To: Chief Surgeon, 1st Army.
Subject: Appreciation of Efficiency Medical Department During Recent Operations.

1. The Army Commander has observed the efficient manner in which your department has handled its numerous duties in connection with our recent operation and especially those *relating to evacuation*. He appreciates fully the difficulties under which these duties were carried out and therefore desires you and the officers and

men under your command to know how much their work has assisted in the success of our operation.

2. Please have the contents of the above paragraph conveyed to the officers and men of the Medical Corps of the Army.

(Signed) H. A. DRUM
Chief of Staff.

The Army ambulance service brought to the railhead hospitals 126,523 sick and wounded; by the 60 cm. and 1 metre railways 1,775. That is a total of 132,605 sick and wounded. In addition they distributed 4,307 medical personnel and their baggage. It evacuated from the Army hospitals on the standard gauge railways 151,045 sick and wounded. That is, the Army evacuation service handled 283,650 sick and wounded cases. In other words, it accomplished the movement of more than a quarter of a million of men. The ambulances traveled 907,910 kilometers, an average of 20,000 kilometers a day.

The Value of Economy of the Ambulance Resources. The success of the Army plan for the evacuation of the wounded depended upon a correct triage, a sufficient mobile motor transportation and the will to see it through. All useless expenditure of ambulances and personnel were cut down, not with any idea of curtailing service or of interfering with the established privileges of hospitals and divisions, but with the idea of having every possible ambulance on hand for the vital effort. The frittering away of ambulances and personnel in providing small details, or humoring the whims of some divisional or hospital commander, was done away with. All the medical motor transport of the First Army was pooled and placed under the command of the Ambulance Director. The medical department of the First Army had the honor of being the first corps to reorganize and put to practice the vital principle of pooling their motor transport facilities. In this way the medical motor transport was made liquid and every wheel kept turning. The key of the situation was that the mass of ambulances was kept in the hands of the Chief Surgeon, with full freedom to group and re-group the units as necessity arose.

THE INTERNIST LOOKS AT THE PROSTATE GLAND

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The invitation on the part of The Mount Sinai Hospital authorities to participate in the dedicatory issue of the hospital journal honoring Doctor Edwin Beer, is a welcome privilege. This delightful act of recognition to our distinguished colleague is a well merited attestation to an honorable, a highly constructive and brilliant career. Reflexively, it reveals those responsible for the institution's destinies to be an appreciative and high minded group. Moreover, it disproves the generally accepted belief that institutions are devoid of soul.

The relator of the medical history of the past ten years will fail to find any subject so thoroughly discussed, and with such conflicting viewpoints, as the therapy of prostatism. If, therefore, as is the case, so much confusion exists within the specialty, what must be the state of mind of the medical man on the side lines? An attempt, therefore, at clarification of some phases of the matter in as detached and disinterested a manner as may be compatible with the human equation, should prove constructive.

The term "internist" will be interpretated to include any qualified practitioner of medicine, general or special. Inasmuch also as the physiology, pathology and therapy of the prostate are so intimately interwoven with that of the adnexa, they, too, will be considered in so far as they have a bearing on the subject.

My readers will not, I trust, consider it facetious when the claim is made here that the five centimeters representing the posterior urethra, which bears an intimate interrelationship to the verumontanum, seminal vesicles and prostate, is the most important segment of the human body. For while it is admitted that the cardiovascular system, the intra-abdominal organs, the ductless glands, etc., possess something more than academic interest, the anatomical segment, under discussion here, is vital. After all, what is the life of a single individual compared to the procreation of the many?

Those who believe that personality is largely dependent upon endocrine balance should recall that an engorged, hyperesthetic verumontanum is frequently the aftermath of superintellectual man's efforts at the regulation of man's most important physiological function. For his own delectation or for some real, generally fancied socio-economic reason, various artifices are interposed in the regulation, prolongation or frustration of, what nature intended to be an uninterrupted businesslike procedure.

Such presumption is inevitably rewarded by a train of psychic phenomena, neuroses etc., which are quite obvious to the initiated, and which in turn have their effect on personality. Curiously enough, while the veru is not histologically speaking, abundantly supplied with erectile or nerve tissue, it must bear, nevertheless, an intimate relation to the sympathetic nervous system. Where the psychic ends and the local lesion begins in what might be called pseudo-impotentia, for example, only the Lord knows; and this knowledge has not as yet been communicated to enquiring man. It is a matter of frequent observation that some of the practices rather euphemistically described above, are the direct cause of profound sensory and psychic disturbances—so much so, in fact, that the associated psycho-neurotic stigmata are quite characteristic. One finds these individuals depressed, apathetic, apprehensive, sluggish in their reaction to environmental stimuli, hypotensive, with subnormal basal metabolism, a lowered capacity for work, and a depressing influence on their immediate circle. These unhappy individuals, and there are many of them, constitute a challenge to the general profession. They certainly should not be dismissed as neurotics or hypochondriacs. Bore into a so-called neurotic case history, habits, physical and chemical findings, long and scrutinizingly enough, and you will find a precise etiological background and a working basis for salvage, or at least amelioration.

In the management of such cases the history is frequently the most important factor. He who would treat these cases with even measurable success must explore the remote recesses of his patient's mind, must bring out in detail habits or practices, business, domestic life, financial difficulties, etc., that may have a bearing on the case. Examination of such a patient constitutes a severe tax on the examiner's professional equipment. The usual so-called complete physical, basal metabolism, biochemical study of blood, urine and stools, and microscopic and cultural studies of prostatovesicular secretion, are routinely carried out. The neuropsychiatric status is an integral part of such a case workup. Finally, an endoscopic examination where not contraindicated, may simplify what might otherwise seem a complex clinical problem.

The treatment, of course, is dependent upon the findings. In general the first step is the treatment, where necessary, of the female of the species. Your gynecological colleague now enters the picture. What is the mental approach? Is the degree of frigidity or torridity, as the case may be, plus, minus or 1–2–3–4 plus? The presence or absence of vaginismus, congenital malformations, etc.—Does the initiative for the practices described arise here? As a pure aside, it is claimed by some psychologists that there is no such thing as frigidity in women, that it is wholly a question of compatibility. There may very well be, and frequently are, factors in this aspect of the case that can defeat the best intentioned efforts. The treatment of the patient proper is local, constitu-

tional and mental. If these patients could be transformed from the condition of morbidity, the depression complex which they so frequently manifest, into a state of euphoria, much of our difficulties would be solved. The local treatment of a congested, hypersensitive verumontanum, in expert hands, is simplicity itself—the same kind of treatment with strong silver solutions or similar preparations, as the practitioner might apply to a congested uvula, and as directly applied and under as precise vision, through an endoscope. Here, however, it should be remembered that an ischemia replaces the hyperemia where the treatments are too long continued. It should also be emphasized that such treatments, inexpertly carried out, damage rather than repair. Of course, there are other pathologic conditions of the verumontanum such as papillitis, residual infections in the utricle, etc. which are not considered here.

GENERAL TREATMENT

To enter into detailed consideration would render this communication too involved and burdensome; moreover, it is unnecessary to a modern audience. Suffice it to state that the findings indicate the selective corrective steps, prophylaxis and habit correction, as a matter of course. One of the most important factors is hypotension. A patient with a blood pressure fluctuating around 100 to 105 systolic is not likely to go places clinically or otherwise. Glandular therapy has a definite place here, especially when administered intravenously, at least so it seems to us. How much a part this type of therapy plays in enhanced potency we have yet to learn. All sorts of empirical gland combinations have been recommended, at first from slaughter houses, later from manufacturing drug emporia for the last fifty years; each year a new empiricism is perpetrated. The rule of common sense will continue to withstand the interested commercialized advice that clutters one's desk. In this connection it should be stated that much is anticipated from the work of *Lower* of the Crile Clinic, *Hinman* and others who, with the necessary mental equipment, laboratory facilities and the even more important clinical background, are conducting interesting researches along this line. Obviously, therefore, the verumontanum, though small in stature, looms large in clinical, economic and sociologic potentiality.

THE SEMINAL VESICLES

The fact that the ejaculatory ducts empty through the verumontanum, and since the lymphatic system and the ducts proper furnish the chief avenues of infection of these structures, the seminal vesicles cannot be considered as an entity apart from the verumontanum. It has been stated that the deep urethra is the mirror of the prostate and seminal vesicles. Primarily, the seminal vesicles are a potential source of constitutional

infection. For the arthritides of Neisserian origin there have been advocated in the past such radical surgical procedures as seminal vesiculotomy, vesiculectomy, vaso-punction and injections of various bactericidal agents, etc. Our conception of this serious and disabling condition is that the newer methods of biological, chemical and instrumental attack are more rational and effective; that, except in the occasional case, there should no longer exist the necessity for mutilating operations. When it is realized that instrumental dilatation of the ejaculatory ducts and lavage of the seminal vesicles is feasible in at least 80 per cent of cases, it would appear that, for the most part, cutting operations in this field, should be relegated to the limbo of antiquarian surgery. This technical procedure was placed on a practical basis by the writer some years ago, since which time we have been able to collect the isolated vesicular secretions unmixed with that of the prostate, to culture the same and to condemn or dismiss this organ as the case may be, as the underlying cause of constitutional disease. My associate, Dr. J. Sidney Ritter, in a joint study of the unmixed seminal vesicular secretion made a few years ago, succeeded in isolating the following bacteria:

1. Nonhemolytic streptococcus
2. Streptococcus hemolyticus
3. Streptococcus viridans
4. Staphylococcus albus
5. Diphtheroid bacilli
6. Staphylococcus aureus
7. An unidentified gram-positive coccus was reported on several cultures; Von Lietenberg states that he found a similar organism in his studies.
8. In five cases, though pus cells were demonstrated in the smears, cultures were negative.
9. In one case, proven to be tuberculous, no organisms were seen in the secretion.

Low grade seminal vesiculitis or inadequate drainage of this sac may be the sole cause of obscure backache, and of vicarious pains in the lower extremities. Subacute or active seminal vesiculitis can be the occasion of many of the manifold evidences of a focal infection elsewhere. It should not be forgotten, however, that, while vesiculitis or prostatitis may reflect remote disturbances, the latter may likewise be the cause of prostatitis or vesiculitis. The treatment of vesiculitis in the acute and subacute stage is palliative; rest in bed, bland diet, hot rectal irrigations, suppositories of codein, belladonna, aspirin, etc. The treatment of the low grade or chronic variety is first, topical application to the verumontanum, mild vesicular massage at regular intervals, vaccine, foreign protein or thermal therapy, as the case may be. For the protracted, the non-responsive variety, separate and culture the segregated vesicular secre-

tions, identify the presence or absence of associated low grade prostatitis, make seminal vesiculograms, and treat according to the findings by means of instillations or lavage of the vesicles and coincidental dilatation of the ejaculatory ducts, etc.

THE PROSTATE

This gland may be invaded by direct extension from the posterior urethra or metastatically through the hematogenous route. As might be expected, many of these low grade infections are the aftermath of antecedent Neisserian infection in 30 to 50 per cent of cases, but rarely does one find the gonococcus in cultural studies of prostatic secretions. In a small series recently studied by us the results were as follows. A case under present observation with a negative prior history and no urinary manifestations, was referred to us to rule out the prostate, as no focus was found elsewhere. We were surprised to find the microscopic field covered with pus cells. Culture of this secretion developed the colon bacillus of the lactic acid type. *Drummond* isolated the trichomona vaginalis in the prostatic secretion of six husbands who had no urinary signs whatever. Their respective wives, however, were under treatment at the time in the gynecological department. The usual results were noted—temporary cure followed by recurrence, repeated treatments and check-up. These men were treated by direct intraprostatic injections after the method devised by the writer. The result in all six was that in curing these men no further recurrence of trichomona had been noted in their wives. A very limited but thought-provoking study.

The following table taken from an investigation by *Dr. Charles Lippow* under the supervision of the writer, indicates the frequency and variety of bacterial invasion of the prostate gland:

Streptococcus:
    Streptococcus Alpha 21
    Streptococcus Hemolyticus 9
    Streptococcus Non-hemolytic 11
    Streptococcus Green 11
Diphtheroids 13
Staphylococcus Albus 22
Staphylococcus Aureus 5
Negative 6
Gram-positive Diplococci 17
Gram-positive Micrococcus 1
Bact. Coli Acidi Lactici 3
Bact. Coli Communis 1

'The reaction to litmus of pyuric urines is of value also, inasmuch as bacteria are highly selective as to the media in which they thrive. It is likewise inadequate to have a knowledge merely of the fact that a urine

is alkaline or acid. The hydrogen-ion content of urine will certainly be a routine observation in the medicine of the immediate future, and such empirical laboratory reports as faintly acid or decidedly alkaline will be rejected. By alkalinization of the urine an environment highly unfavorable to certain types of bacterial activity is produced; so too with hyperacidulation. These estimations are of considerable importance especially in the administration of various medicaments. Nor should the continued promiscuous administration of acid or alkaline therapy, especially in debilitated individuals, be practiced without concomitant knowledge of the CO_2 combining value of the blood, for the very good reason that such patients may thus unwittingly be thrown into a condition of acidosis or alkalosis.'

The foregoing commentary, first made by the writer some five years ago, is exceedingly interesting in the light of present day practice in the administration of such new drugs as Prontylin and the Mandelates. As a matter of fact, the average laboratory report on the quantitative estimation of the Ph. content of the urine, may, because of the time element, be worthless. Such estimations should be routine in the physician's office. The technique is simple and accurate enough for practical purposes—Nitrazine paper with colorimetric chart or chlorophenol red with color tubes similar to phthalein. The latter, according to one of my associates, is particularly valuable in the range between 5.5 and 6.8. Such tests can be carried out by any intelligent person. Thus it becomes apparent that we are now entering a new and fascinating field of the therapy of urinary infections, with rationalized and precise methods, and a reasonable prospect of definitely better results.

The manifold sources of prostatic infection, local and remote, venereal and non-venereal, the vaginal flora, the infectious diseases and the constitutional repercussions of these infectious foci in the muscles, joints, heart, even the eye, are proved clinical facts. Moreover, competent observers believe that 30 to 50 per cent of all male mankind from 40 years upwards (we support higher figures) are the carriers of low grade infection.

The internist, the practitioner of general medicine, who seeks possible infectious foci in teeth, tonsils, gall-bladder, appendix, etc., meanwhile overlooking the prostate, is comparable to the general defending a position, who erects fortifications on his front and sides, leaving his rear exposed.

OBSTRUCTING PROSTATISM

Any attempt at clarification of this muddled situation is, to say the least, timely. Not so many years ago, the problem as it presented itself to the profession outside of urology was about as follows. Twenty-five or more per cent of individuals from 55 years on, presented themselves with symptoms of increasing disability, frequency, especially nocturia, hesitancy at the onset of the act of micturition, diminished projectile

force, prolongation of the act and terminal dribbling—the clinical picture of beginning prostatic obstruction. If treated at all, only palliative measures were employed. Generally speaking, operative interference, because of its gravity, was all too frequently not given serious consideration until the patient had reached the point of intolerance, wherein any alternative was welcomed. This situation was unfortunate for the reason that in the interim, the disabling sequelae of obstructing prostatism supervened, the patient's resistance was lowered and the mortality rate thereby increased. Happily, conditions have changed for the better. In recent years advances have been made in instrumental methods of correction of obstructing prostatism that are little short of revolutionary. The same vicissitudes have attended this as are common to all innovations —enthusiasts in whose hands these new methods have practically replaced open cutting operations; a middle-ground group who regard instrumental methods as supplemental and not a replacement of the longer established open surgical procedures; a third, perhaps smaller group, who employ it in a very limited number of cases, if at all. It has been somewhat facetiously, if descriptively, depicted as a geographical matter. In the corn and cotton belt many urologists have "gone overboard" on the method and have laid the scalpel away. In the citrus belt an intermediate position is a fair estimate; while in the "effete east", though the number of advocates is constantly growing, open surgery has the call in the majority of cases. The following quotation by the writer is taken from a communication in the Journal of Urology, September 1937, page 307, chapter 2:

"It has been interesting to note the varying trends of the time. In an increasing number of the larger clinics, a degree of enthusiasm is manifested for closed surgery, which at least equals that of the original proponents of these methods. The conclusion to be drawn from this situation is, that while technical ability, judgment, etc., are vital, a fine organization is of equal importance. Such, at least, is the deduction of the writer. Individuals, it should be pointed out, or the occasional adventurer in this field of endeavor, cannot hope to achieve such results. The other extreme of viewpoint is represented by a group of urologists of unquestioned ability who relegate this type of surgery to a relatively minor rôle. Paradoxically as it appears, both are right. This last mentioned group has developed a high degree of skill in open surgery; results in their hands are better than with other methods. Such individuals must either elect to serve a more or less prolonged apprenticeship, a period fraught with travail, with a coincidental higher mortality, developing facility with technical methods to which they may not be adaptable, either temperamentally or by past experience. One elects to do that which one does best whether it be tight-rope walking or steeple climbing. In this transitional period, prostatics will perhaps be all the better for the pursuit of this practice."

There are three major factors involved in the operative approach of whatever type. First, the physical status of the patient which includes, of course, hemoglobin, blood count, blood grouping, blood sugar, degree of nitrogen retention, and the acid base balance of the blood. Second, the type and degree of obstruction. Third, when present, the type and extent of underlying associated infection. Too much emphasis has been placed on the second and too little upon the third major factor. Practically all these prostates are infected in greater or lesser degree. Occasionally, this gland is the site of discrete foci of pus; calculous disease is encountered from time to time. There are two obvious implications here; the first is for a more scientific approach, a precise knowledge of the bacteriology and, where indicated, preparatory efforts at its correction or amelioration. The second, it seems to us, exposes the fallacious position of the pan-instrumental prostatectomists. In this evolutionary period a reasonable middle-ground is sound advice—see to it that the method is allocated to the case rather than the case to a method.

Whatever the pros and cons of the management of established prostatic obstruction, there is no valid reason why a patient should experience the disastrous sequelae of obstructing prostatism. Once a patient manifests increasing disability, a nocturia, residual urine of an ounce or more, and when endoscopic examination reveals beginning obstruction, then when these conditions are present, and are not responsive to palliative measures, it should be recognized that we are dealing with a progressive lesion in a retrogressing patient. This is the time to give serious consideration to the advisability of instrumental correction. Herein lies a great opportunity for constructive sociological endeavor. The profession at large should cease regarding these manifestations as a normal concomitant of senility. The prophylaxis of obstructing prostatism will undoubtedly constitute the major phase of its surgical therapy in the years to come.

LYMPHOSARCOMA OF THE PROSTATE

With Report of a Case

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[From the Urological and Pathological Services of the Brooklyn Hospital]

Tumors of the prostate other than carcinoma are relatively rare and practically all of the cases reported have been some form or another of sarcoma. Randall and Hughes (1) writing in 1929 analyze one hundred cases of prostatic sarcoma found in the literature and, like other authors, reflect considerable doubt on the accuracy of the diagnosis, especially in many of the older case reports. They are particularly skeptical of the seven cases of lymphosarcoma in this group, feeling that some, at least, were really examples of very anaplastic carcinoma. Ewing (2) previously had expressed doubts concerning the few reported cases of lymphosarcoma, stating that "the structure of the gland does not favor the occurrence of such tumors." Randall and Hughes were unable to find any lymphoid tissue in sections of many normal prostates. Symmers (3), on the other hand, contends that the prostate belongs to a so-called auxiliary lymphoid system and that, like the suprarenal capsule, thyroid, lung, liver, kidney, testicle and other organs, the prostate normally contains interstitial lymphoid foci which may easily be overlooked but, in certain cases of disease, can be readily identified. A tumor, according to Symmers, might spring from such foci.

Ferguson and Stewart (4) suggest such a pathogenesis in a case they reported in 1932 in which there had been an old gonorrheal infection, and they call attention to the fact that in some of the other cases reported there was also a history of an antecedent gonorrhea. (This was also true of our own case, reported in this paper.) They say, however, that it is their impression that nodular lymphoid accumulations are somewhat less frequent in the prostate than in the bladder base.

Lowsley and Kimball (5), writing in 1934, report on one hundred and thirty-two cases of prostatic sarcoma reported in the literature and add one case of leiomyo-sarcoma.

Townsend and Kobisk (6), writing in 1935, add thirteen other cases to those reported by Lowsley and Kimball, including a case of their own; a case of fibrosarcoma. Ferguson and Stewart (4) in the article referred to above report a case of lymphosarcoma of the prostate and review the literature. They found only four previous cases which they were willing to accept as proven lymphosarcoma:

I. Coupland's (7) case reported in 1877.
II. Kaufmann's (8) case reported in 1902.
III. Quinby's (9) case reported in 1920 and
IV. Symmers' (3) case reported in 1923.

In a recent personal communication Ferguson (10) reports two other cases observed by him since the publication of his paper. In one of these the data are insufficient to warrant including. The other case was a man of 30 who for four weeks had complained of pain in the right lumbosacral region, accompanied by marked frequency of urination and dysuria. Rectal examination showed a large, firm, somewhat elastic mass which practically filled the pelvis and replaced the prostate. Aspiration biopsy showed lymphosarcoma. He was subjected to X-ray therapy with some apparent improvement at first, but later failed rapidly and died eight months after the beginning of symptoms. Autopsy showed "extension to the peritoneum and mesentery causing practically complete intestinal obstruction."

All of the cases reported have been rapidly progressive and universally fatal. The outstanding symptoms have been frequency, dysuria, occasionally, but not always, hematuria, and lumbar and sacral ache. Rectal examination in all cases showed a large elastic, smooth and regular enlargement of the prostate differing very materially from the findings noted in cases of carcinoma which are characteristically hard and nodular. Our case reported somewhat in detail was as follows:

History. The patient was a widower, aged 52, admitted to the Brooklyn Hospital on April 3, 1937. His family history was negative. In his youth he had gonorrhea which lasted several months He thought that he was eventually completely cured and he had had no further symptoms directed to his urinary organs until at the beginning of his present illness. Many years ago he was operated upon for fistula in ano and had a very prolonged recovery. Several years ago he contracted pulmonary tuberculosis He was discharged from a sanatorium four years ago with the pulmonary lesion apparently controlled. He was then in apparently good health until six months ago when he noted a little difficulty in urination; the stream was small and very slow in starting. This condition grew slowly worse until two weeks ago, when it became very much aggravated. He had been catheterized several times in the last week, each time with difficulty and followed by considerable bleeding. For several weeks he had also suffered from a vague sense of distress in the upper left abdominal quadrant and had "had a lot of gas". He had lost a little weight in the past six months.

Examination. His general appearance was that of a man in fairly good health. The heart sounds were normal. Examination of the lungs showed some dullness at both apices with bronchovesicular breathing and a few crepitant râles. The prostate was moderately large, smooth

and regular and slightly hard. The median furrow was practically obliterated. There were two small nodules in the rectal wall with a dimple between them directly over the prostate. These were interpreted as scars of the old fistula in ano. The residual urine varied from nothing to complete retention. Cystoscopy under sacral anesthesia showed a mild cystitis, a moderately trabeculated bladder wall, a very heavy prostatic median bar and moderate intraurethral intrusion of the lateral lobes. The provisional diagnosis was prostatic carcinoma.

Laboratory Data. The urine showed much pus and many red blood cells. Cultures showed colon bacilli. The Wassermann test was negative. The blood chemistry showed: urea, 27.39 mgm. per 100 c.c.; creatinin, 2.44 mgm.; sugar, 149 mgm. A blood examination revealed: hemoglobin, 70 per cent; red blood cells, 3,800,000; white blood cells, 8,200; polymorphonuclear neutrophiles, 72 per cent.

Phenolsulphonphthalein excretion was 74 per cent in three hours with a good curve.

The blood pressure was 150 systolic and 90 diastolic. Temperature, pulse and respiration were normal.

X-ray examinations of the lumbar spine and pelvic girdle were negative for any evidence of metastases but it was noted by the radiologist that the intestines on the left side of the abdomen were markedly distended with gas.

Operation (April 6, 1937). Under spinal anesthesia the median bar was resected transurethrally and six radium seeds, averaging $2\frac{1}{2}$ mc. each, platinum screened, were implanted in the prostate through the perineum and a bilateral vasectomy was done. He made a smooth recovery from this operation. The indwelling catheter was removed in twenty-four hours, following which he voided normally and had practically no further symptoms referable to his bladder. The pathological findings of the fragments of prostate removed were as follows: Several of the fragments showed partial or complete replacement of the prostatic tissue by a diffuse, infiltrative neoplastic growth, the cell type of which was a rather large lymphoblast. In many fields remnants of prostatic acini were found within densely packed sheets of tumor cells (Fig. 1). Under low magnification the cells appeared quite uniform in size and shape but higher magnification revealed considerable anaplasia. Mitotic figures were very numerous.

Course. On April 8, 1937 a fragment of the rectal nodule was removed for histological examination, which showed tumor tissue of exactly the same appearance as that in the prostate gland (Fig. 1).

It seemed reasonable to assume, at least tentatively, that the tumor had arisen in the prostate and extended to the rectum, although the extreme rarity of primary lymphosarcoma of the prostate was appreciated.

Dr. James Ewing was requested to examine the sections of rectal and

prostatic tissue and his reply was "I think your tumor of the prostate and rectum is certainly a lymphosarcoma."

The patient was discharged from the hospital on April 14, 1937 feeling very comfortable so far as his bladder was concerned, but still complaining of considerable abdominal distress. It was planned at this time to have him return later for deep X-ray therapy.
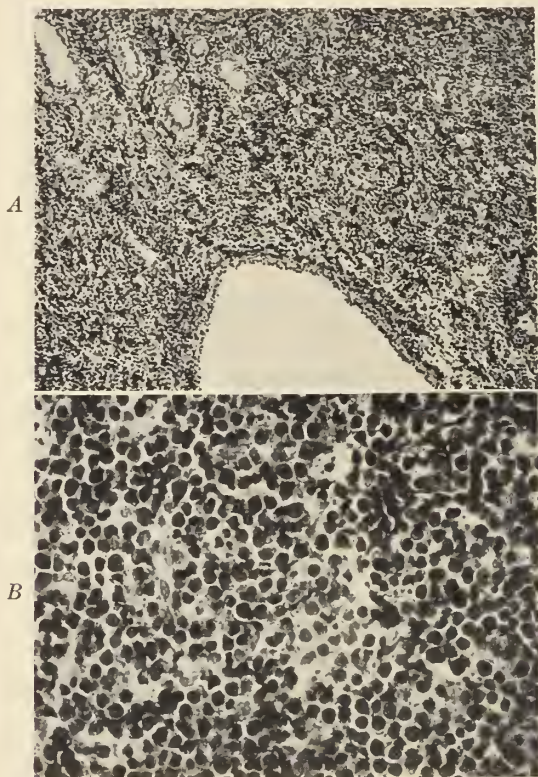
FIG. 1. (A) A portion of the biopsy specimen from the prostate showing remnants of gland acini surrounded by a diffuse infiltrative growth. (B) A characteristic high-power field taken from the rectal biopsy specimen, showing tumor cells intermediate in size between the small and large lymphocyte. Many hyperchromatic nuclei and a number of mitotic figures can be distinguished. The cells are rather regularly distributed in a scanty stroma.

Following his return to his home his abdominal distention and distress grew progressively worse and he was readmitted on April 21, 1937 with definite indications of partial intestinal obstruction. A barium enema on April 22, 1937 was essentially negative. A barium meal on April 23, 1937 showed a definite obstruction somewhere in the jejunum. In spite of conservative measures the obstruction was progressive and finally complete. He was operated upon on that day by Dr. E. K. Tanner. A tumor was found involving the jejunum with partial intussusception and complete

obstruction at the site of the tumor. This was widely resected with a lateral anastomosis.

The specimen removed showed the following (Fig. 2): In the center of a resected portion of the jejunum was a tumor mass arising from a zone 2.5 cm. in length, encircling the wall and replacing all but the serous coat. The lumen at this level was reduced to a narrow cleft lined by neoplastic tissue. The growth varied from 0.5 to 3.5 cm. in thickness so that the

Fig. 2. The resected tumor-bearing portion of the jejunum showing partial intussusception and a high degree of obstruction. The small cleft to the left of the midline is all that remains of the lumen.

lumen was eccentric. The tumor-bearing portion had been partially intussuscepted and hung as a polypoid mass in the lumen of the inferior portion of the gut. On section the tumor tissue was pearly white and homogeneous. In the mesentery a large lymph node was found which seemed to contain neoplastic tissue. Microscopic sections of the intestinal growth and the enlarged node showed tumor tissue of the same appearance as that in the prostate and rectum.

He apparently stood the operation fairly well but grew progressively

weaker and in spite of the usual supportive measures, including a trans-
fusion, died forty-eight hours after operation. An autopsy was obtained.

Necropsy Findings. The body was that of a middle-aged, well developed
and moderately well nourished male. The skin and mucous membranes
of the eyes, nose and mouth showed nothing remarkable. The abdomen
was markedly distended and tense. A recent right rectus incision was
found with the sutures in position and the wound edges well approximated.
There was no evidence of wound infection. Examination of the thorax
and abdomen was made by opening and enlarging the surgical incision.

A small amount of fibrinous exudate was found among the loops of
intestine. A lateral anastomosis of the jejunum was found at the site of a
surgical resection. The anastomosis was in good condition, with signs of
early healing. It was located approximately two and a half feet below
the jejunoduodenal junction. The jejunum proximal to this site was
markedly distended, of a dark red color, and was extremely flaccid. The
bowel distal to the anastomosis was very hyperemic. For a considerable
distance above and below the anastomosis the intestine contained hemor-
rhagic fluid. The mucosa of the proximal portion was elevated from the
underlying coats, forming large gas-filled blebs. Several slightly enlarged
lymph nodes were found in the mesentery.

The liver was of normal size and shape. It was of a pasty tan color and
its markings were somewhat obscured by fatty degeneration. There was
no gross evidence of tumor tissue.

The *gall-bladder* and extra-hepatic biliary passages were grossly normal.

The *spleen* was moderately enlarged and its capsule was thin. On
section the splenic tissue presented the appearance of so-called subacute
splenic tumor.

The *pancreas* and adrenals were grossly normal.

The *kidneys* were of normal size and shape, their capsules stripped
readily and their surfaces were smooth. On section the renal tissue showed
marked cloudy swelling. The pelves were not dilated, and the ureters
were thin walled, of normal calibre and showed no inflammatory changes.

The *bladder* (Fig. 3) was empty. The wall was moderately hyper-
trophied, and a slight amount of purulent fluid covered the mucosal
surface. At the neck of the bladder there was a small elliptical zone of
ulceration with a slightly elevated indurated margin. The ulceration
extended slightly into the prostatic urethra.

The *prostate* (Fig. 3) was greatly enlarged, measuring 6.5 cm. trans-
versely, 4 cm. anteroposteriorly, and 4.5 cm. in its vertical diameter. It
was rather firm in consistency. On section the prostate tissue was found
extensively replaced by a new growth. The tumor occurred in islands
with irregular outlines. The central portions of these islands were of a
violet color, while the margins were pearly white, homogeneous and
translucent. The intervening prostatic tissue appeared normal. From

the posterior surface of the prostate the tumor extended into the rectal wall and protruded into the lumen in the form of two rounded masses each with a transverse diameter of about 2 cm. They were elevated about 1 cm. above the level of the surrounding rectal mucosa. In the center of one of these nodules was an ulcerated area the site of recent biopsy.

Fig. 3. The entire contents of the pelvis resected at autopsy, showing the enlarged prostate cut transversely and the proximal portion of the urethra and the bladder laid open by an interior midline incision. A small elliptical ulceration is seen at the bladder neck, the site of resection of a "prostate bar." The bladder wall is moderately hypertrophied.

Both testicles were grossly normal.

The pleural and pericardial sacs contained slightly more fluid than normal.

Both *lungs* were adherent at the apices by dense fibrous adhesions. At the right apex the pleura measured .5 cm. in thickness, and beneath this area

FIG. 4. The rectum opened by a posterior incision. Two nodular protrusions are shown in the center of the picture. The one toward the left shows a partially healed biopsy wound.

FIG. 5. A cross section through the prostate and rectum. At "A" is shown one of the rectal nodules seen in Figure 4. Pearly grey tumor tissue occupies most of the section. The dark patches are areas of hemorrhage and necrosis, the result of the insertion of radon seeds. The tumor tissue in the rectum is continuous with that in the prostate.

a small cavity, filled with caseous material was found. The left apex showed a thinner pleural scar and a cavity smaller than that on the right. Scattered fibrotic and calcified tubercles were found throughout all of the lobes. The intervening lung tissue was emphysematous and congested.

The *heart* was of normal size and shape. Its walls were of normal thickness and the chambers were not dilated. All of the valves were grossly normal. The coronary vessels showed only slight sclerotic changes. The ascending aorta was the seat of marked arteriosclerosis. At several points the intima was ulcerated and a soft, recently formed thrombus was attached to one of these ulcers. The thrombus projected as a polypoid mass into the lumen of the vessel.

No enlarged *lymph nodes* were found except, as noted above, near the site of resection of the jejunum.

Histological study of sections from numerous portions of the various viscera showed no tumor tissue except as grossly noted. Cross section of the entire prostate and adjacent rectum showed extensive replacement of the prostate with tumor tissue and continuity between this and the nodules in the rectum. The histologic appearance of the neoplasm was identical with that noted in the operative specimens.

DISCUSSION

The case herein reported, we believe, is undoubtedly an example of lymphosarcoma of the prostate, a lesion very rarely encountered and probably even more infrequent than the number of the cases, so classified in the literature, would indicate.

The likelihood that some, or even most, of the cases reported in the past were, in reality, instances of very anaplastic carcinoma has been discussed by the more recent writers on the subject, to whom reference has already been made. In the few evidently authentic examples of lymphosarcoma involving the prostate, one is impressed with the lack of conclusive evidence that the neoplastic process actually originated in that organ. Several explanations for this situation seem possible. Perhaps, as Ewing has intimated, there is no such entity as primary lymphosarcoma of the prostate. The seeming absence of lymphoid tissue from the normal organ supports this viewpoint. On the other hand the ubiquitous distribution of lymphoid structures throughout the body suggests that small foci may be present occasionally in the prostate, although not ordinarily observed. If Symmers' concept of the prostate as an auxiliary lymphoid organ be correct, one would expect to find that organ implicated quite regularly, like the lungs, liver and kidneys, in the various "lymphomatoid diseases." This convenient designation was suggested by Krumbhaar (11) for the group of diseases including the leukemias, Hodgkin's disease, lymphosarcoma and other related processes.

Another explanation of the lack of conclusive evidence that lympho-

sarcoma is ever primary in the prostate may be drawn from a consideration of the nature of this particular neoplastic process. It is a disease not of separate organs but one of lymphoid tissue common to many organs. It occurs far more frequently as a regional or widespread sarcomatosis than as a single discrete tumor formation. Often the apparently simultaneous involvement of whole systems of lymph nodes or of a long segment of intestine suggests multicentric or diffuse malignant proliferation, rather than origin from one isolated lymphoid focus.

In our case there was found a large prostatic lesion continuous with two small nodules in the adjacent rectal wall. There was no involvement of seminal vesicles and only slight implication of the neck of the bladder. The possibility that this pelvic lesion was a metastasis from the tumor in the jejunum seems difficult to accept but perhaps not more so than the converse interpretation. The remote possibility of the tumor having been primarily in the rectum and having extended to the prostate hardly seems worthy of serious consideration. We feel that the lesions in the prostate and jejunum may reasonably be considered as independent coincidental neoplasms.

The clinical significance of this whole problem rests very largely upon the fact that this type of tumor is supposed to be, in fact is, highly radio-sensitive and it would seem reasonable to assume that an early diagnosis and proper treatment might succeed in materially modifying the course of this intensely malignant disease.

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OBSERVATIONS ON THE CLINICAL PICTURE AND THERAPY OF DIVERTICULITIS OF THE COLON

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Close upon thirty-four years ago Edwin Beer published one of the first comprehensive reports on acquired or false diverticula of the intestine (The American Journal of the Medical Sciences, 137: 135–140, July 1904). He supported the view which is still more or less generally accepted today that these pouches result from increased intra-intestinal pressure, in which the straining of constipation may play a rôle, through natural defects such as vascular openings or through weakened areas in the muscular wall of the gut due to the atrophy of age. Although he was only able to collect eighteen cases from the literature at that time, his classical analysis of the pathological and clinical aspects of the condition did much to crystallize the conception of it as a definite entity and gave a tremendous impetus to its study. Since then many papers on diverticulosis and diverticulitis have been written and thousands of cases have been reported, but as yet not much, except the fact that the condition is a relatively common one, has been added to Beer's contribution. In spite of many statistical studies based on a wealth of material, an accurate diagnosis of the disease is frequently impossible and the correct decision as to what is the proper therapeutic procedure in a given case is often very difficult.

Diverticula may be found in any portion of the intestinal tract. Acquired diverticula and those which are most prone to inflammatory disturbance and its serious complications occur, however, most commonly in the colon, particularly in the descending colon and sigmoid. In many instances, they give no trouble for years and are often only diagnosed as an incidental X-ray finding, are accidentally discovered during a laparotomy done for some entirely independent condition, or are found at a post mortem examination, having no causal relation to the death. We propose to discuss briefly our impressions of the clinical picture and therapy of diverticulitis of the colon, based on twenty-six cases, personally observed at Lenox Hill Hospital during the past twenty-two years. All cases without symptoms or signs of inflammation and all involving the appendix and the small intestine have been excluded for the purposes of this report.

The average age for the group was fifty-three and one-quarter years. The youngest patient was twenty-eight, the oldest seventy years. The sexes were equally represented, there being thirteen female and thirteen male patients. Only six patients of the group were seen on the public

ward, the remainder being private patients. Other observers have also noted that patients with diverticulitis are more commonly seen in private practice than among ward cases.

The "gall bladder" type of individual is apparently also very prone to have diverticulitis. Most of our patients were over-weight, some being markedly obese. The obesity and its associated fatty infiltration of the colon may be a factor in the weakening of the gut wall and the formation of the diverticula.

After studying the histories of these patients and analyzing a carefully prepared chart of the series, one is impressed by the fact that there is no clear-cut syndrome characteristic of the malady. The symptoms presented have been so variable and perplexing that it is no wonder that a definite diagnosis could not often be made.

Pain was the most common complaint, and was present in all of the cases. The type, location and duration of the pain, however, varied greatly. The symptom of pain was distributed as follows: generalized, eight cases; left lower quadrant, seven cases; entire lower abdomen, six cases; right lower quadrant, two cases; left upper quadrant, umbilicus, and rectum, one case each. Most patients complaining of generalized and lower abdominal pain seemed to show an emphasis of the discomfort on the right side. In some, the pain was sharp and knife-like. In others, it was very slight. In some cases the complaints were present over a period of years in the form of recurrent attacks. In others, the complaint was present for only several hours. Some patients were only slightly uncomfortable and were able to carry on with their work. In others, the discomfort was severe enough to incapacitate the patients. There is apparently no typical radiation of the pain, nor is there any relation to meals.

The next most common complaint was related to bowel movements. Twelve of the patients were chronically constipated. Only three gave a history of normal daily bowel movements. In the others there was a history of occasional sluggishness and attacks of diarrhea. Two patients noticed that their stools were becoming narrow, while four developed more or less acute intestinal obstruction. Only one gave a history of bloody stools. In connection with this, we may say that it is our impression that blood-streaked stools are more common in carcinoma than in diverticulitis, and this sign is more apt to be of diagnostic aid in the former than in the latter condition.

Distention was complained of by five patients. It was present in several of the others who were acutely ill. Nausea and vomiting were found only in those cases which presented signs of a peritonitis or intestinal obstruction. Chills and fever were not consistent complaints in our series, except in the really acute inflammatory cases.

The physical findings were as confusing and as varied as the subjective

complaints. In most of the patients there were peritonitic signs, tenderness, rigidity, and rebound tenderness and tympanites, varying in degree from those found in a mild local irritation or a definite walled off abscess to those characteristic of a progressive or even very urgent generalized condition. If localized, they were usually more marked in the lower abdomen, and very often they were more pronounced in the right lower quadrant than in the left. In the obstructed cases these were the usual signs of abdominal distention, visible peristalsis and enterospasm. Except in those cases where a mass was present, rectal (including sigmoidoscopy, which if attempted, must be done with the utmost care for obvious reasons) and vaginal examinations did not yield much information. The leucocyte count, as a rule, was analogous to that found in appendicitis. If the inflammatory process was acute and the patient's resistance good, there was a marked leucocytosis. If the infection was particularly virulent, there was a relatively high polymorphonuclear percentage with a distinct shift to the left. In some of the rather active cases, however, an almost normal white blood cell count was obtained.

Eighteen of the cases in our series were operated upon and the remaining eight were treated medically. In the latter group the patients gave vague histories of abdominal pains and aches varying from several hours to several years in duration. Two of these were seen when acutely ill, but the physical findings in these, as well as in the remaining six of the group, showed nothing more than slight abdominal tenderness. The diagnosis, while suspected, was not proved until X-ray examination showed the presence of intestinal diverticula.

The preoperative diagnoses in the surgical group varied as follows: acute appendicitis, eight; appendiceal abscess, one; carcinoma of the sigmoid, three; peritonitis of unknown origin, two; strangulated hernia, one; intestinal obstruction of unknown origin, one; and acute diverticulitis, two. While diverticulitis was thought of as a possibility in connection with all of these cases, nevertheless the clinical pictures presented would not have justified such a diagnosis. As yet the only means of being certain of its presence is by X-ray examination or by the findings at operation or autopsy. The condition, however, is undoubtedly rather prevalent and should always be borne in mind in questions of differential diagnosis of an acute abdomen. It should always be looked for at operation if the other findings do not satisfactorily explain the clinical picture and the surgeon should always be prepared to deal appropriately with the condition.

It might be worth while at this point to emphasize again the importance of the X-ray examination in these cases. The best method of showing the lesions is by the barium enema. Of course this cannot be done while patients are acutely ill, but, when possible, the examination should be done following a thorough preparation. This should consist of a dose of castor oil the night before, and a soapsuds enema the next morning. A

light breakfast is permitted. With the patient on the fluoroscopic table, a small amount of barium is allowed to enter the lower sigmoid. The examiner should note the mobility of this section of gut. This is most important because the perisigmoiditis may be so extensive as to fix the sigmoid completely. A larger amount of barium may now be allowed to flow in, and the outlines of the colon noted. A very common finding in these cases is the presence of a spastic colon. Often the diverticula will not be seen until after defecation, at which time the residual barium will be seen to lie in the pouches of the diverticula. Air inflation may be of some help, but will not be found as useful in these cases as in other types of pathology of the large gut. Differentiation from carcinoma is sometimes difficult, but usually possible.

Of the eight cases treated medically, all recovered and are now in good health after periods varying from six months to five years with no major recurrences. The treatment in these cases consisted of absolute bed rest for periods varying from several days to several weeks. The institution of a bland, low residue, non-irritating diet was very essential. All attempts were made to obtain at least one normal stool daily. Frequent rectal examinations were necessary to obviate fecal impaction. Where such a tendency existed, mineral oil by mouth and the instillation of warm olive oil by rectum were used. A glycerin suppository was often needed to start a movement but even small low enemas were rarely given. In certain instances deep X-ray therapy over the diseased area seemed to be beneficial. These cases should be given a clear understanding of the malady for which they are being treated. It is only in this way that the full coöperation of the patient can be obtained and the more serious consequences of diverticulitis prevented. Should recurrences take place in spite of conservative treatment, such as outlined above, surgery may become necessary. The correct indication in these cases, if technically feasible, would be an ileosigmoidostomy, or better still a transverse colosigmoidostomy, with or without proximal exclusion of the diseased segment. A colectomy with a resection of the entire area affected, though theoretically, perhaps, the ideal procedure for a radical cure, is too critical an operation to be seriously considered in the treatment of recurrent diverticulitis except, possibly, under the most unusual circumstances.

Of the eighteen cases of diverticulitis operated upon, all with obvious surgical indications, thirteen recovered and five died. They may be grouped pathologically, quite in line with Beer's early classification, into:

1. Peridiverticulitis and penetration into mesentery with localized peritonitis, one.
2. Peridiverticulitis and perforation with localized intraperitoneal abscess, two.
3. Peridiverticulitis, with or without perforation, with spreading peritonitis, six.

4. Peridiverticulitis and perforation with diffuse fibrinopurulent peritonitis, five.
5. Sigmoiditis and perisigmoiditis with inflammatory tumor producing stenosis of the intestinal lumen, five, in one of which there had been a previous perforation, localized abscess and secondary fecal fistula above the stenosis.
6. Sigmoiditis and perisigmoiditis with dense adhesions to the urinary bladder, two. Both of these cases are also included under 5.

The following procedures were instituted: Exploration and drainage with appendectomy, eight. All of these cases recovered. In one patient a perforated diverticulum was closed, the pelvis was drained and the appendix was removed. He recovered. We, however, no longer consider this advisable. Usually the gut wall is so edematous that the sutures cut through, and if sutures are taken at some distance laterally, there is danger of narrowing the lumen. When such a situation is encountered, and the involved bowel is freely movable and easily exteriorized, this is much more satisfactory and less dangerous, and should be utilized. In one patient with a solitary penetrating diverticulitis of the ascending colon a primary resection was done, successfully. One patient, in whom a cecostomy was done, expired on the tenth day after operation from a pulmonary embolus, confirmed by post mortem examination. In seven patients, exteriorization was performed. Four of these cases died, three before resection and one in whom resection was done purely as an ante mortem attempt to relieve the patient. In two of these cases, in which the diagnosis of carcinoma was made even at operation and only disproved by subsequent examination of the tumor, the bladder was inadvertently opened in separating the very adherent sigmoid from it. The bladder openings were closed successfully and apparently this accident was not in any way responsible for the fatal outcome in either case. The cause of death in one of these cases was peritonitis from a beginning intraperitoneal gangrene of the upper limb of the sigmoid loop due to devitalization in mobilizing the gut—an ever present hazard in every exteriorization operation. The other three cases died of sepsis from retroperitoneal phlegmons, the result of the extensive manipulation in freeing the fixed infected sigmoid from the posterior abdominal wall. The remaining three cases in which exteriorization was done as a primary procedure recovered. In two of these, subsequent resection of the diseased gut and closure of the colostomy was done. In one of these two cases, until the actual microscopic study of the resected specimen, malignancy was regarded as the probable diagnosis. In the third case in which the appendix had also been removed, the perforation was closed and the exteriorized loop replaced in the abdominal cavity. A fourth successful secondary exteriorization, resection and closure of the colostomy was done on one of the cases in which a right iliac abscess had been drained and a persistent, intractable

Table of Cases

NUMBER	NAME	AGE	SEX	YEAR	PAIN Duration	PAIN Site	STOOLS	STATURE	SIGNIFICANT PHYSICAL FINDINGS	X-RAY EXAMINATION	DIAGNOSIS, PRE-OPERATIVE	FINDINGS AT OPERATION	TREATMENT—OPERATIVE PROCEDURE	PATHOLOGICAL CLASSIFICATION	RESULT
1	T. K.	54	M	1916	48 hrs.	R. L. Q.		Heavy	T. 99.2	P.-op. exam.; divert. of sigmoid	Acute appendicitis	Perforated diverticulum; perisigmoiditis; pelvic abscess involving mesentery	Appendectomy; repair of perforation; drainage of abscess	2	Cured
2	R. K.	68	F	1924	24 hrs.; cramps	General abd.	Obstipation 4 days	Over-weight	Distended; diffuse tenderness; fibroid uterus	Obstruction of sigmoid; probably carcinoma	Obstruction; ca. of sigmoid?	Sigmoid tumor; ac. divert.; mesenteritis; adherent to bladder; uterine fibroid	Separation of adhesions; opened bladder easily closed; exteriorization; drainage of pelvis	5 + 6	Died, 48 hrs. p.-op.; gangrene of upper limb of exteriorized intestine; peritonitis
3	R. F.	46	M	1925	2 wks.	Lower abd.		Heavy	T. 103; lower abd. tender, rigid; rectal, tender in cul-de-sac		Appendiceal abscess	Diverticulitis of sigmoid; abscess mass in mesentery with firm adhesion to bladder	1st op., drainage of perisigmoid abscess; appendecectomy. 2nd op., sigmoidectomy; 2 stages	5 + 2	Cured
4	A. K.	56	F	1927	1 yr.	Rectum	Constipation	Obese		Divert. of colon and sigmoid	Chronic obstruction	Diverticulitis of colon and sigmoid; peritonitis	Cecostomy	4	Died, 10th day p.-op. Autopsy showed pulmonary embolus
5	W. B.	59	M	1931	5 wks.	Lower abd.; left back	Narrow, bloody, 14 days	Heavy	Mass, L. L. Q.	Obstruction of sigmoid	Obstruction; prob. ca.	Inflammatory sigmoid mass; perisigmoiditis; obstruction of sigmoid	Resection of sigmoid; 2- stage. Several closures of fecal fistulae	5	Cured

No.	Name	Age	Sex	Year	Duration	Location	Bowel habit	Build	Clinical findings	Pre-op. diagnosis	Diagnosis	Operative findings	Treatment	No.	Result
6	R. G.	45	M	1931	5 days; also 1 yr. ago	Lower abd.	Constipation	Obese	T. 102.6; rebound tenderness; rigidity; mass in lower abdomen			Perforated divert. of sigmoid into mesentery; obstruction; peritonitis	Exteriorization	5	Died, 5th day p.-op. Sepsis; retroperitoneal phlegmon
7	E. K.	58	F	1932	3 mos.; cramps	General abd.	Constipation	Obese	Distended	Partial obstruction of sigmoid	Chronic ileus; prob. ca.	Large inflammatory tumor of sigmoid; frozen to bladder	Division of adhesions; opened bladder easily closed; exteriorization; ante-mortem resection	5 + 6	Died, 2nd day p.-op. Sepsis; retroperitoneal phlegmon
8	F. N	28	M	1933	24 hrs.	Lower abd.	Normal	Overweight	Diffuse abdominal tenderness		Acute appendicitis	Perforated divert. of sigmoid; peritonitis	Appendectomy; drainage	3	Recovered
9	M. B.	64	F	1933	3 days	General abd.	Diarrhea, 3 days	Obese	T. 101.5; tender, rigid, distended	P.-op. exam.; diverticulitis of colon and sigmoid	Acute appendicitis	Diverticulitis with perisigmoiditis and mesenteritis; peritonitis	Drainage of pelvis; appendectomy	4	Recovered
10	M. O.	46	F	1933	Several hrs.	L. L. Q.	Normal	Obese	Tender, L. L. Q.	Spasm; divert. of sigmoid	Diverticulitis	Perforated divert.	Medical	3	Symptom-free
11	I. B. C.	46	M	1933	Past yr.; 2 mos. ago; 24 hrs. ago	General abd. and rectum		Obese	T. 102.6	P.-op. exam.; diverticulitis of sigmoid	Acute appendicitis	Diverticulitis and perisigmoiditis	Appendectomy; drainage; perisigmoiditis	3	Recovered
12	C. H.	43	M	1934	6 wks.; slight; 10 days severe	L. L. Q. to rectum	Chronic constipation		T. 100; distended	Divert. of sigmoid	Diverticulitis		Medical		Symptom-free
13	M. L.	35	F	1934	2 yrs.; severe for 24 hrs.	R. L. Q.	Constipated	Well nourished	T. 100.4; tender, R. L. Q.; rt. fornix		Acute appendicitis	Penetrating diverticulum of ascending colon	Ileo-cecal resection, one-stage	1	Cured
14	M. McG.	70	F	1935	24 hrs.	General abd.	Chron. constipation; very severe for the past month		Irreducible femoral hernia; lower abdominal tenderness		Strangulated hernia	Diverticulitis of sigmoid; perforation; fecal peritonitis; obstruction	Exteriorization with drainage, secondary resection	4	Cured
15	O. P.	50	M	1935	Past yr.	General abd.	Diarrhea	Slim	Weight loss; abdominal soreness	Divert. of sigmoid	Diverticulitis		Medical		Symptom-free

Table of Cases—Concluded

NUMBER	NAME	AGE	SEX	YEAR	PAIN Duration	PAIN Site	STOOLS	STATURE	SIGNIFICANT PHYSICAL FINDINGS	X-RAY EXAMINATION	DIAGNOSIS, PRE-OPERATIVE	FINDINGS AT OPERATION	TREATMENT—OPERATIVE PROCEDURE	PATHOLOGICAL CLASSIFICATION	RESULT
16	A. L.	60	F	1935	20 yrs.	L. L. Q.	Very frequent attacks of diarrhea	Overweight	Lower abdominal spasm	Divert. of sigmoid	Diverticulitis		Medical		Symptom-free
17	A. R.	45	M	1935	6 hrs.; severe cramps	General abd.	Normal	Very well nourished	Tender, R. L. Q.	Divert. of sigmoid	Acute appendicitis	Perisigmoiditis; adhesions. Partial obstruction of small intestine	Appendectomy; drainage	3	Recovered
18	H. C. S.	65	M	1936	52 hrs.; colic	L. L. Q.	Slight constipation		T. 99; tender, rigid, L. L. Q.	P.-op. exam.; divert. of sigmoid	Acute Diverticulitis	Inflammatory sigmoid mass; perisigmoiditis; diverticulum perforating into mesentery	Appendectomy; drainage of pelvis	3	Recovered
19	E. D.	50	F	1936	18 hrs.	Lower abd.	Constipated	Slightly overweight	T. 101.4; tender, rigid, L. L. Q.	P.-op.; divert. of sigmoid	Peritonitis	Perforated divert. of sigmoid; diffuse peritonitis	Appendectomy; exteriorization of perforated sigmoid; drainage; later closure of fistula	4	Recovered
20	H. B.	50	M	1936	12 hrs.	Umbilical region	Diarrhea 3 days; constipation 4 days	Heavy	T. 101; rigidity and rebound tenderness in R. L. Q.	P.-op.; divert. of colon and sigmoid	Acute appendicitis	Inflammatory tumor of sigmoid extending into mesentery	Appendectomy; drainage of left pelvis and perisigmoiditis	3	Recovered
21	E. R.	36	F	1936	2 wks.; severe	L. U. Q.	Markedly constipated	Very obese	Diffuse abdominal tenderness	Divert. of sigmoid	Chronic diverticulitis		Medical		Symptom-free
22	W. N.	69	M	1936	3 days; cramps	Lower abd.	Constipation and diarrhea 4 days; narrow stools past yr.	Overweight	T. 103.4; distended; rebound tenderness, lower abdomen		Acute diverticulitis	Mass in left pelvis due to perforated diverticulitis of sigmoid	Exteriorization	3	Died, 3rd day p.-op. Sepsis; retroperitoneal phlegmon

No.		Sex	Year	Duration	General abd.	Constipation	Very obese	Tenderness	Diverticulitis	Diagnosis	Findings	Treatment		Result
23	E. C.	59	F	1936	4 days; also many yrs. ago		Constipated 4 days		Tender, L. L. Q. distended		Chronic diverticulitis		Medical		Symptom-free
24	E. W?	60	F	1937	1 wk.; cramps	L. L. Q.	Chron. cons.; blood, mucus			Divert. of sigmoid	Diverticulitis		Medical		Symptom-free
25	A. G.	66	M	1937	2 days	L. L. Q.	Constipated	Obese	Tender, lower abdomen; also vaginally		Acute appendicitis	Diverticulitis and perisigmoiditis; dense pelvic adhesions and peritonitis	Appendectomy; drainage	4	Recovered
26	A. S.	56	F	1937	3 yrs.; slight	L. L. Q.	Normal	Over-weight	Slightly tender, L. L. Q.	Spasm; divert. desc. colon and sigmoid	Diverticulitis		Medical		Symptom-free

fecal fistula with an inflammatory stenosis of the gut below necessitated the radical operation. All the surgical cases which recovered have remained well since operation, as regards their diverticulitis and as far as we have been able to follow them, for from eight months to sixteen years. Naturally, all these patients were put on a strict postoperative regime, similar to that instituted for those patients who were treated only medically, but it seems probable that the rather remarkable freedom from symptoms following simple drainage is due largely to the protective and isolating effect of the adhesions which must form around the involved gut after the subsidence of the acute inflammatory process.

As mentioned above, in three cases the diagnosis of carcinoma of the sigmoid was made before operation and only positively disproved after resection by microscopic examination. We have also had the reverse experience on several occasions, a preoperative diagnosis of diverticulitis proven at operation or by subsequent study of the resected specimen to be carcinoma. We have not, however, although by no means denying the possibility, ever observed any etiological connection between diverticulitis and carcinoma.

It will be noted that our operative deaths occurred in those patients in whom there had been much manipulation at operation. In those cases where a minimum amount of surgery was done, recovery resulted. We have therefore come to the conclusion that the less one does surgically, the more chance the patient has of recovery. If on exploration a diffuse pelvic peritonitis and cellulitis with an extensive perisigmoiditis and marked adhesions are found, it is best to institute drainage, and nothing more, preferably even omitting the appendectomy. Of course, where symptoms of obstruction are present, a colostomy or cecostomy is indicated, with drainage of the diseased area, as needed. If a colostomy is done, it is important that only that portion of the gut well above the disease, such as the transverse colon, which can be freely delivered into the wound without extensive separation of adhesions should be used. After a time the inflammatory process will subside, the diseased area will become more mobile, and even the stricture may tend to open as a result of the diversion of the fecal current by the colostomy. The colostomy can then be closed, but if X-ray studies still show sufficient disease or obstruction after a reasonable interval, some form of safe resection can be done in a quiescent period as a secondary procedure.

CONCLUSIONS

1. Diverticulitis of the colon is not an uncommon condition and, as Beer also emphasized in his early paper, should always be thought of in a patient, especially one after middle life, suffering from an acute abdominal disturbance. It is a very serious malady, often with a protracted morbidity and a high death rate.

2. The positive diagnosis of the disease is still very difficult notwithstanding many clinical and pathological studies, based on a wealth of material, that have been made on the subject in the past thirty-four years. Actually the only moderately definite preoperative diagnostic pointer is the X-ray examination by barium clysma, and this can only be used in a quiescent stage of the disease.

3. Ultraconservatism should be the therapeutic watchword. Medical treatment should be instituted at first, if possible. If progressive peritonitic or obstructive symptoms and signs or the suspicion of malignancy force a resort to surgical intervention, the least radical operative procedure compatible with the findings should be adopted.

FRIEDLAENDER BACILLUS INFECTIONS OF THE URINARY TRACT

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The frequency and the clinical significance of B. friedlaender infections of the urinary tract is not generally appreciated. In the experience of our hospital, it is the second most frequent site of infection with this organism. This report is concerned with fifty-two cases of B. friedlaender infection of the urinary tract which were encountered among two hundred consecutive infections of various parts of the body.

Like many other organisms encountered in the urinary tract, B. friedlaender belongs to the intestinal flora. According to Dudgeon, (1) B. friedlaender is found in the stools of 5.5 per cent of persons. Kendall (2) considers the organism an almost constant habitant of the intestinal tract of nurslings, common in the intestinal contents of bottle fed infants and frequently found in the adult intestinal tract. It is therefore not surprising that our experience indicates that the B. friedlaender is most commonly encountered in intraabdominal suppurations due to perforative lesions of the intestines and the appendix. Our series of two hundred infections includes sixty-one cases of this type. The relative number would probably have been even larger were it not for the fact that surgeons frequently failed to take cultures in cases of intraabdominal suppuration caused by appendicitis and other forms of intestinal perforation.

The most probable explanation for the fact that this has not been the common experience in all hospitals is that the organism frequently fails to be identified by the bacteriologist because of certain biological similarities to B. coli. We are so accustomed to finding B. coli in genito-urinary infections and in appendicitis pus that any gram negative bacillus is apt to be immediately inoculated into the various sugar media in order to differentiate it from other members of the colon-typhoid group. Unfortunately, B. friedlaender forms acid and gas on the same sugar media as some of the commoner stains of B. coli. Unless a capsule stain is made or the mucoid character of the surface ground on solid media is noted, the organism may be confused with the colon bacillus.

Another explanation for errors in identification of the organism in genito-urinary infections is the fact that B. friedlaender has been associated for seventy-five years in the minds of physicians with infections of the

respiratory tract, and is still regarded as a common cause of pneumonia. In our experience the lung is one of the rarest sites of infection. And yet the organism continues to be called the bacillus pneumoniae or the pneumobacillus, and even its scientific designation is Klebsiella pneumoniae.

This traditional but erroneous association of the organism with pneumonia is due to the fact that Friedlaender (3) discovered his organisms in 1880 in post mortem spreads from pneumonic lungs. They probably represented a post mortem contamination with intestinal contents or a secondary preagonal invasion. At that time the cause of lobar pneumonia was still unknown and Friedlaender's organism was therefore called bacillus pneumoniae. It was not until Weichselbaum's (4) work four years later that the cause of lobar pneumonia was proved to be the diplococcus pneumoniae of Fraenkel.

In our fifty-two cases of B. friedlaender infection of the urinary tract, pure cultures were obtained in thirty-nine instances, and mixed cultures with one or more organisms in the remaining thirteen. The organisms

TABLE I

B. Friedlaender Infection (200 cases)

SITE	NUMBER OF CASES	MORTALITY	BACTERIEMIA	
			Number	Died
Gastro-intestinal tract	61		1	1
Biliary passages and liver	46	14 (30%)	6	5
Genito-urinary tract	52	9 (17%)	7	4
Vagina, uterus and adnexa	6		1	1
Lungs and upper respiratory tract	25		1	1
Miscellaneous, skin, meninges, etc	10		1	1

commonly observed in association with the Friedlaender bacillus were B. coli, B. alkaligenes, B. pyocyaneus or the enterococcus. These organisms, like the Friedlaender group, are primarily derived from the intestinal flora, indicating a close similarity in their mode of infection.

As in the biliary system, mechanical factors which cause urinary stasis predispose the urinary tract to infection. In thirty-eight of our patients with B. friedlaender infection urinary calculi were encountered; carcinoma of the bladder in one case, adenoma of the prostate in two cases, tuberculosis in two cases, papilloma of the bladder in one case, horseshoe kidney in one case and kinking of the uretero-pelvic junction in one instance. Only in six cases of the series of fifty-two was no mechanical urinary stasis demonstrable.

B. friedlaender not infrequently gains entry from the intestinal tract into the blood stream of the portal or the systemic circulation. From the portal blood it is excreted by the liver and passes through the biliary tract without giving rise to infection unless there is biliary stasis due to

calculi, neoplasm or some other obstruction. Similarly, the organisms which enter the systemic blood stream are excreted by the kidney and usually pass through the urinary passages without inducing an infection unless there is some mechanical cause for stasis. In this connection it is interesting to note that most of our cases of severe hepatic or biliary tract infection with bacteriemia developed a secondary excretory infection of the urinary passages.

The prognosis of infections of the urinary tract is grave. Although the mortality is by no means as high as in biliary tract infections with this organism, nine cases of the fifty-two died of their infection, a mortality rate of 17 per cent. In four of the nine fatal cases, a bacteriemia was demonstrated by blood cultures during life.

TABLE II
B. Friedlaender Infections of the Urinary Tract (52 cases)

Pure culture	37
With B. coli, B. alkaligenes, B. pyocyaneus or enterococcus	13
Predisposing urinary stasis	44
Urinary calculi	38
Carcinoma of bladder	1
Prostatic adenoma	2
Tuberculosis	2
Horseshoe kidney	1
Kinking of uretero-pelvic junction	1
Papilloma of bladder	1
Fatal cases (Mortality 17%)	9
With bacteriemia	4
Bacteriemia	7
Fatal (Mortality 57%)	4

We have encountered seventeen cases of B. friedlaender bacteriemia. Of this number, seven arose from infections of the urinary tract. This includes two instances in which the organism was recovered from the blood stream only on the day following instrumentation which had precipitated a so-called urethral or ureteral chill. Another patient recovered after having had two positive blood cultures.

In one of the four fatal cases, the patient recovered spontaneously from the bacteriemia and was discharged from the hospital apparently cured. He returned eight weeks later because of the sudden collapse of a vertebra due to a metastatic osteomyelitis. From this secondary osteomyelitis focus of infection there developed a reinvasion of the blood stream with B. friedlaender to which the patient succumbed.

In another of the four fatal cases, a cystoscopy was followed almost

immediately by daily chills and fever.   This case is so characteristic of the
mode of development of bacteriemia and its consequences that it is re-
ported in detail.

ILLUSTRATIVE CASE

History (Adm. 409035).   The patient was a 72 year old Hungarian born
male, admitted to the Surgical Service of Dr. E. Beer on May 24, 1937.
Family and past history was irrelevant.   Four years before his admission
to the hospital, he began to be incontinent of urine.   He was cystoscoped
in The Mount Sinai Hospital Out-Patient Genito-Urinary Clinic and
a papilloma of the bladder was discovered.   The tumor was fulgurated
and urinary control was fully re-established until six months before
entrance to the hospital.   At that time he again had incontinence asso-

TABLE III

B. Friedlaender Bacteriemia (17 cases)

Fatal cases..(Mortality 80%)	13
Pure culture..	14
With B. coli..	1
With several bacteria..	2
Portals of entry:	
Liver and biliary tract	6
Urinary tract..........	7
Otitis media, mastoiditis and meningitis	1
Post laminectomy meningitis	1
Gynecological tract.......	1
Intestinal tract (preagonal in aplastic anemia)	1
Recovery:	
Liver and biliary tract	1
Urinary tract..........	3

ciated with a dull aching pain in the lower abdomen.   He was submitted
to cystoscopy and the bladder papilloma was found to have recurred.
It was again fulgurated.   The last cystoscopy was performed four weeks
before admission.   Following the last instrumentation he developed daily
chills and fever which continued until the time of his admission four weeks
later.

Examination.   The patient was a well developed and obese male who
did not appear acutely ill.   Bilateral costovertebral tenderness was
present and the prostate was noted to be moderately enlarged and firm.
Blood pressure was 130 systolic and 60 diastolic.   The diagnosis made
on admission was recurrent papilloma of the bladder and acute
pyelonephritis.

Laboratory findings.   Hemoglobin 93 per cent, white blood cells 22,000

with 88 per cent polymorphonuclear neutrophiles of which 71 per cent were segmented forms and 17 per cent non-segmented forms. The urine was cloudy, acid in reaction, contained 2 per cent sugar, no albumin; microscopically many white cells and occasional pus clumps were noted. Blood urea was 14 mgm. per 100 c.c. Blood Wassermann reaction was negative. Phenosulphonphthalein test revealed 30 per cent excretion of dye in five hours. Electrocardiogram showed left axis deviation, P3 was inverted, QRS slurred and low in amplitude, Q1 present; Q4 absent; RT transition elevated in leads 1 and 2. T1 semi-inverted; T2 and T3 are low in amplitude. Roentgen examination of the chest was negative.

Course. During the first four days of hospitalization, the patient's temperature ranged between 100–103 degrees F. daily. Three days after admission because of the clinical and electrocardiographic evidence of recent coronary artery thrombosis the patient was transferred to the Medical Service. Two days later, local pain and tenderness developed one inch below the right nipple in the anterior axillary line, together with flatness, absent breath sounds and fremitus in this area. There was no foul breath, chest pain or expectoration. X-ray examination of the chest now revealed a collection of fluid in the lowermost portion of the right pleural cavity without any evidence of an intrinsic infiltrative lesion. Four days later re-examination of the chest showed no change.

During this period however, a diabetic condition which was discovered on admission became increasingly difficult to control. The temperature fluctuated between 99–101 degrees F. Aspiration of the right axilla was performed on several occasions yielding cloudy fluid with 3600 white cells and 6750 red cells. Gram stain of this fluid showed no organisms. Culture of the fluid was reported five days later as showing a B. friedlaender, while culture of the urine also revealed B. friedlaender. Blood culture taken four days later was reported as containing B. friedlaender in one flask.

As soon as these reports were available, surgical consultation was requested. On that day X-ray examination of the chest showed a slight diminution in the fluid in the right pleural cavity with an area of increased aeration in the axillary portion. This was thought to represent a loculation of air within the adhesions of the pleura, which might be the result of aspiration. It was impossible, however, to exclude the presence of an abscess of the lung. Thoracotomy for empyema was performed two weeks after admission and a pocket containing six ounces of thick viscid yellowish green pus was found under the axillary portion of the right lower lobe. Behind this and laterally was a pocket containing 300 c.c. of thin greenish fluid. For the first week after operation, he seemed well, the temperature gradually seeking a lower level. However, he became weaker, markedly debilitated and presented an increasing tendency to cyanosis. He died ten days after operation and four weeks after admission.

In retrospect, the sequence of events responsible for the development of the bacteriemia was first the fulguration of the bladder papilloma with resulting cystitis. The traumatization of cystoscopy then provided the entry into the blood of the bacillus of Friedlaender which was probably already present in the bladder. The bacteriemia was responsible for a metastatic lung abscess which ruptured and formed a putrid empyema.

SUMMARY

The urinary tract is the second most frequent site of infection with the bacillus of Friedlaender. Fifty-two B. friedlaender infections of the urinary tract were encountered in two hundred infections of various parts of the body. The number is only exceeded by the frequency with which the organism is encountered in appendicitis and other perforative lesions of the intestinal tract.

The organism usually enters the blood stream from the intestine and is excreted through the urinary or the biliary tract. It is therefore frequently found in association with other organisms similarly derived from the intestinal flora. With few exceptions, it fails to cause an excretory infection unless there also exists a mechanical predisposing factor, such as a calculus, neoplasm, malformation, etc., which favors stasis. Bacteriemias from other primary sites of infection, such as the liver and biliary tract, usually cause a secondary excretory infection of the urinary tract.

The mortality rate of primary B. friedlaender infection of the urinary tract is high, 17 per cent. In the nine fatal cases, death was due to bacteriemia in four.

Urinary tract infections are the most frequent primary sites of B. friedlaender bacteriemias. Among seventeen cases of bacteriemia with this organism, seven arose from a genito-urinary infection. Of this number, three recovered from the blood infection, two after a single positive blood culture following a urethral or ureteral chill and one after two positive cultures.

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PAPILLOMA OF THE CHOROID PLEXUS OF THE FOURTH VENTRICLE

CASE REPORT

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Neoplasms arising from the ventricular structures make but a very small percentage of all brain tumors. Their interest lies not in their rarity but in the fact that, in spite of their location, modern neurosurgery has made them accessible. And by their inherent characteristics of growth and development they offer, once exposed, a much more favorable prognosis for complete extirpation and cure than do many of the more superficially situated growths.

Papillomas arising from the choroid plexus comprise one such group. Their frequency is about 0.5 per cent, based on Dr. Cushing's figures of 2,000 verified tumors (1). He encountered twelve of these growths, of which nine were in the posterior fossa and three above the tentorium. In 1930 Van Wagenen (2), in reporting two cases observed by him in the lateral ventricles, listed those in the literature. Of the forty-seven cases so collected, twenty-three were in the fourth ventricle, seventeen in the lateral ventricles, and three in the third ventricle. In a very excellent review of tumors of the fourth ventricle, Lereboullet (3) devotes a chapter to papillomas arising from the choroid plexus. About twelve more cases (including Cushing's five additional cases) have been reported since Van Wagenen's publication. These are one case each by Guillain (4), Kellner (5), Fehr (6), Obarrio (7), and Montanaro (8), and two by Vincent (9).

CASE REPORT

A recent instance of this interesting type of tumor, successfully operated upon, follows:

A ten months' history beginning with stiffness of the neck. Progressive weakness and instability, cerebellar signs and papilledema. Operative removal of papilloma. Recovery.

History (Adm. 393429). In May 1936 a forty-three year old housewife was admitted to the Neurological Service. She had been well up to July 1935, at which time she noted stiffness of the neck which came on suddenly while she was returning home from a bathing beach. Soon after the onset of this sysptom she noted generalized weakness and unusual drowsiness.

At about the same time dull pain in the supraorbital region and pain in both arms appeared. After a few months all these symptoms subsided, but she did not feel well. In January 1936 she noted transitory blurring of vision on first getting up in the morning, which was at times associated with vertigo. Immediately upon lying down her symptoms would disappear. These complaints continued up to the time of her admission to the hospital. In February a hysterectomy was done at another hospital, and on her return home she noted black spots before her eyes and increased weakness of her legs, which persisted. About a month before her admission her gait became staggering and she complained of pins and needles sensation in her hands.

Examination. The patient walked on a broad base with a tendency to fall constantly to the right. There was occasionaly dysmetria with the right hand, and slight adiadochokinesis with the left hand. The deep reflexes were hyperactive and equal, the abdominal reflexes were absent; no pathological reflexes were obtained. There was bilateral papilledema of 4 to 5 diopters; the left pupil was larger than the right, both reacting better in accommodation than to light. Bilateral weakness of the external recti was present, and a coarse nystagmus was noted to left and right. Forward flexion of the head met with slight resistance. A lumbar puncture was not done; other laboratory tests revealed no abnormality.

Course. Under a diagnosis of a posterior fossa tumor, exploration was carried out on June 4, under avertin and local anesthesia. After a ventricular puncture had shown an internal hydrocephalus, the cerebellum was exposed by means of a curved transverse incision. When the dura was opened it was noted that the cisterna magna contained very little. fluid. When the arachnoid of the cistern was opened a greyish pink tumor was seen overlying the left tonsil. About one-half of the tumor lay above and the rest below the level of the foramen magnum. The right tonsil was herniated into the spinal canal alongside the tumor. Coursing along the mesial side of the tumor was an artery about the size of the lead in a pencil. After clipping this vessel the lower free portion of the growth could be lifted by traction sutures. Its upper end seemed to merge with the tonsil. The lower half was removed in one piece. The remainder, except for a small tab, was excised with suction and the cutting current. The tumor was very vascular. After its removal a free flow of cerebrospinal fluid from the fourth ventricle was obtained on jugular compression.

Microscopic Examination (Figure 1). The tumor was reported by Dr. Globus as follows: Hematoxylin and eosin preparation shows cuboidal and columnar epithelium arranged in more or less definite acini. The columnar epithelial cells are densely packed, the cuboidal less so. Many are in irregular strands with papillomatous outgrowths. The strands of cells frequently enclose a homogeneous, pink-staining material, probably

colloid. There are many calcific deposits, some of which assume the character of psammoma bodies. Occasionally strands of collagenous fibers and connective tissue nuclei are encountered. No cilia, blepharoplasten, or mitotic figures are seen. *Diagnosis.* Papilloma of the choroid plexus.

The postoperative course was without untoward incident. At the time of the patient's discharge the papilledema was receding but the cerebellar signs showed very little, if any, improvement. However, when examined about a year later, the fundi were flat, there was no ataxia, nystagmus could still be brought out on looking to either side, and the left sixth nerve was still weak. Subjectively, the patient felt well. She had gained in weight and was carrying on her usual household duties.
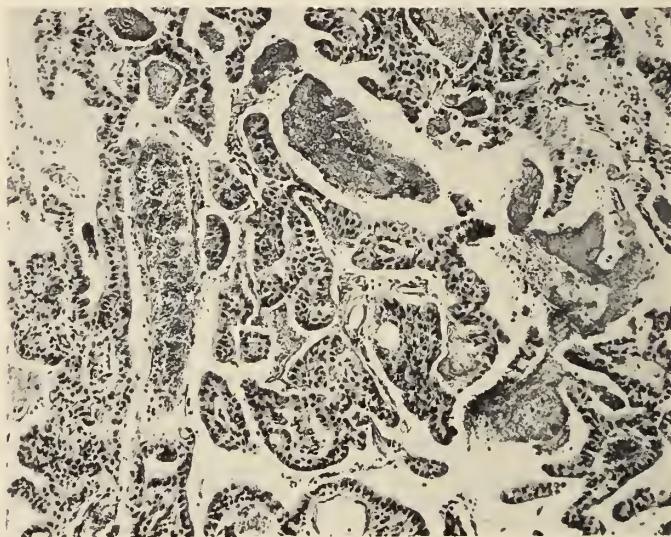
FIG. 1. Section of the tumor, showing its papillomatous organization (Hematoxylin and eosin stain)

Both Van Wagenen and Lereboullet point out that papillomas of the choroid plexus occur more frequently in the earlier decades of life. The latter also noted in fourth ventricle tumors the frequency of complaints referable to the neck and the location of the pain in the supraorbital region, rather than headache. Both of these symptoms were exhibited by our patient, as was weakness, a symptom observed in other reported cases.

In our patient the papilloma extended through the foramen of Magendie to present itself outside the ventricle. In some cases the growth remained confined to the ventricular cavity, while more rarely the tumor originating from the choroid of the lateral recess extends through the foramen of Luschka to appear in the cerebellopontine angle and mimic the symptomatology of an acoustic tumor.

Papillomas of the choroid plexus are non-infiltrating and slow-growing. The unblocking of the fourth ventricle, even without any excision of tumor, is enough at times to give prolonged relief (nearly five years in a case reported by Cushing (1)). The case reported by Sachs (10) was symptom free for five years following excision and lived eighteen months after a second exploration showed multiple implants in the posterior fossa.

The almost complete extirpation made in the case here reported, should afford a long period of freedom from symptoms before a considerable re-growth takes place or distant implants manifest themselves.

SUMMARY

A case of papilloma of the choroid plexus, successfully operated upon, is described. The incidence of this tumor and its characteristics are discussed.

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BLADDER COMPLICATIONS AFTER MAJOR PROCTECTOMY

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One of the most frequently observed complications of the many which follow in the path of either rectal or rectosigmoid resections for carcinoma is that of vesical dysfunction. As a matter of fact it is so common that there are some surgeons who state that it is universally present, varying only in its severity. Yet full reports of bladder complications following major proctectomy have been few (2, 3).

When the anatomical relationship of the urinary bladder to the rectum and rectosigmoid are considered, it is not strange that vesical dysfunction should occur so commonly in the course of major proctectomy. As a matter of fact, it is difficult to conceive how the rectum can be surgically extirpated without doing some damage to the vesical innervation. According to most anatomists, the pudic nerve is the sensory nerve to the urethra and the motor nerve to the external sphincter of the bladder which is further supplied by the four lumbar sympathetic ganglia via the presacral nerve, and by the parasympathetic fibers, via the pelvic nerves derived from the third and fourth, and occasionally the second sacral nerve. Both these sets of fibers form dense interlacing plexuses of nervous tissue called the pelvic or inferior hypogastric plexus. These lie in the lower part of the pelvic cavity on either side of the rectum just where it passes through the pelvic floor.

Nerve fibers from these plexuses course to supply the wall of the bladder, the prostate, the seminal vesicles, the vas deferens in the male, and to the uterus, ovaries and fallopian tubes in the female. Hill and his co-workers (2) state that each lateral half of the bladder is supplied by the corresponding hypogastric plexus. The parasympathetic fibers are more apt to be injured in resections of the rectum than the presacral nerves, which are somewhat more distant to the operative site.

According to Woollard (4), the sympathetic fibers are supposed to be inhibitory to the detruser of the bladder and tonic to the internal sphincter of the bladder, while the parasympathetic fibers produce contraction of the bladder musculature and relaxation of the internal sphincter.

It becomes quite obvious from this brief anatomic description and from a study of Woollard's excellent dissections (Figs. 1 and 2) that some damage must be done to the pelvic nerves in major rectal excisions. On the other hand, because of the extensive and widespread nature of the

nerve supply, complete denervation of the urinary bladder seems almost impossible. In addition, the bladder possesses remarkable ability to rapidly regain its function even after extensive operative manipulations.
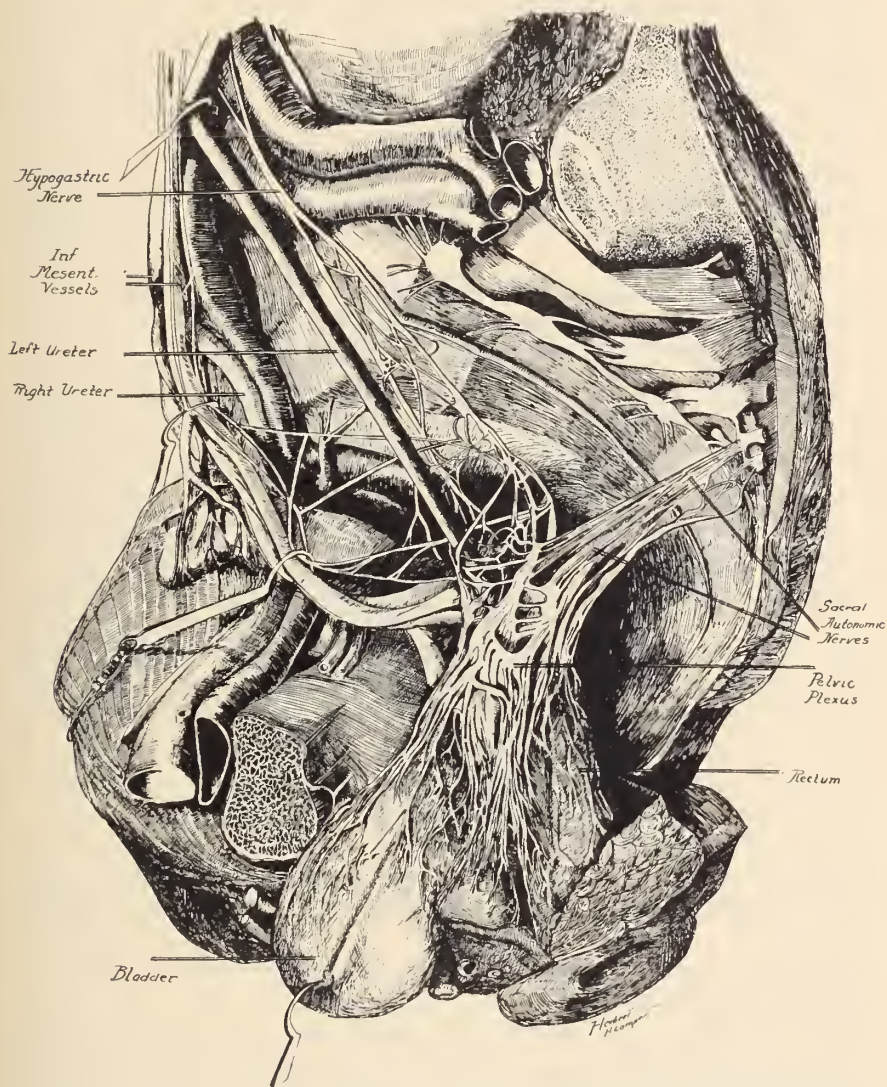
FIG. 1. A dissection showing the distribution of the hypogastric and pelvic nerves (after Woollard).

Theoretically, the operative trauma to these nerves should in a large measure depend upon the location and the extent of the carcinoma, and the amount of lymphatic, perirectal and perisigmoidal infiltration. The damage to the nerve supply of the bladder and the bladder wall itself, might either be insignificant or severe, depending upon the pathology

present and the skill of the operator. The degree of vesical dysfunction; therefore, would vary accordingly from transient postoperative retention to permanent urinary incontinence.

It was thought, therefore, that it might prove of some interest to analyze not only the frequency but also the types of vesical dysfunction following either rectal or rectosigmoidal resections for carcinoma. Accordingly, a series of twenty-six consecutive ward cases from the surgical wards of The Mount Sinai Hospital were studied from this viewpoint. There were fifteen females and eleven males. All of these patients were operated upon in two stages; that is, a preliminary colostomy followed by a radical excision of the neoplasm. Twenty-one were subjected to the Lahey type
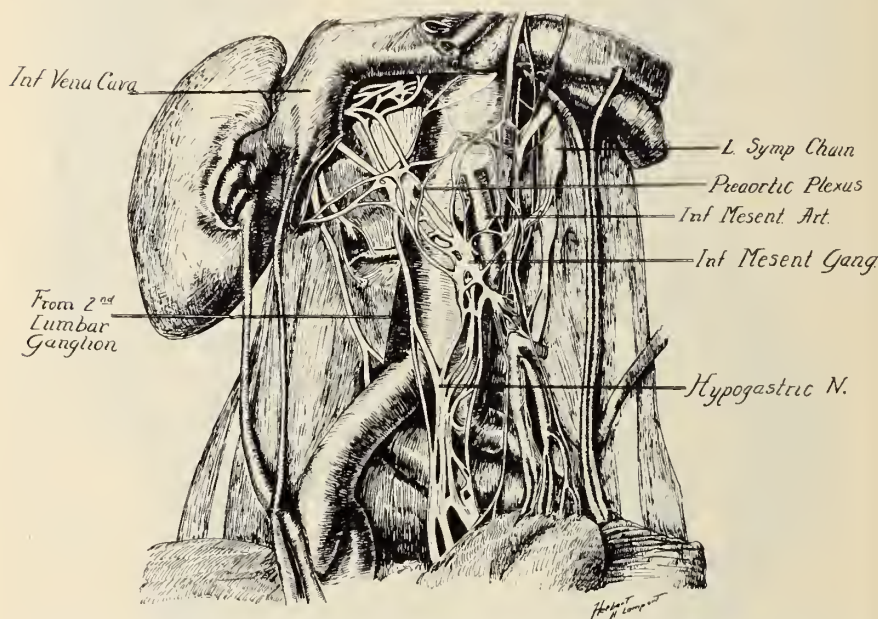
FIG. 2. A dissection showing the position and connections of the inferior mesenteric ganglion and the formation of the hypogastric nerves (after Woollard).

of abdomino-perineal procedure, one to a perineo-abdominal operation, and four to perineal resection.

In this series there were two adenocarcinomata of the rectosigmoid, one of which was infiltrating, and twenty-four malignant neoplasms arising from various parts of the rectum, of which thirteen were infiltrating. In spite of the extensive pathology in more than half of the cases, the urinary complications, although present in the majority, were usually transient and of a mild degree. Death resulted in one case from a gangrenous cystitis. This patient (Adm. 389410) a fifty-nine year old housewife and a rather severe diabetic, died eight days after the second stage of a Lahey procedure for an infiltrating carcinoma of the rectum with lymph

node metastasis. The post mortem report (9869) revealed the following significant pathology. "The mucosa of the ureters presents a dull, hazy, grey appearance. The bladder is distended and partially filled with cloudy straw colored urine. The mucosa is varied in color, consisting of red, yellow and brown irregular non-elevated areas. Microscopic examination of the bladder shows that its entire wall is infiltrated by inflammatory cells. The surface epithelium is completely denuded except for a small area. The mucous membrane is edematous and infiltrated by inflammatory cells. The muscular coat is markedly infiltrated by numerous polymorphonuclear leucocytes, plasma cells, lymphocytes and occasional histiocytes. The vessels of the mucosa are distended and hyperemic with occasional thrombi."

The origin of the cystitis in this case and in many others was probably due to the introduction of infection while catheterizing a traumatized, and either partially or completely paralyzed bladder containing some residual urine. Inasmuch as the bladder is partially paralyzed in practically all of these cases, catheterization is indicated until full function is restored. Since the introduction of infection is always possible and is more likely to be multiplied by repeated catheterizations, not only should the catheterization be meticulously performed by reliable and experienced internes or nurses with the minimal amount of trauma, and under the strictest aseptic precautions, but the number of catheterizations should be reduced by the employment of the indwelling or retention catheter. It is also most important to adequately protect the open end of this catheter against the possibilities of ascending infection from external contamination. It has been our custom in performing any major proctectomy to insert an indwelling catheter in the operating room just prior to operation. In the male, an open end rubber catheter ⚹ 26 French is used, and in the female, a Pezzer catheter ⚹ 14 French is introduced. Not only is the bladder kept continuously empty during the operative procedure, but in the male the catheter clearly outlines and defines the course of the urethra so that the danger of injuring it during the course of the perineal resection is materially reduced.

When the patient is returned to the ward after operation, the retention catheter is immediately connected to an apparatus designed and popularized by Duke of the St. Mark's Hospital of London (Fig. 3). It is a two-way system by which the urine may be eliminated and the bladder may be irrigated and the catheter and the attached tubing kept flooded with an antiseptic solution. Fifty cubic centimeters of a 1–5000 acriflavine solution is instilled every four hours and is retained for ten to fifteen minutes. The urine is then allowed to drain into a sterile receptacle and after the release of the urine the catheter is again sealed with the antiseptic solution. The bladder is irrigated twice a day with warm acriflavine solution 1–5000. The catheters are changed every two or three days

under sterile precautions.   At the end of four or five days the catheter is removed and the patient encouraged to void.   If urination is impossible, the catheter is replaced for another twenty-four hours or until such time as the patient is able to void spontaneously.   The majority of these patients tolerated the catheter quite well.   Four of the patients did complain of some discomfort in the bladder region, but only one patient suffered pain on urination after the catheter was removed.   Examination of the urine
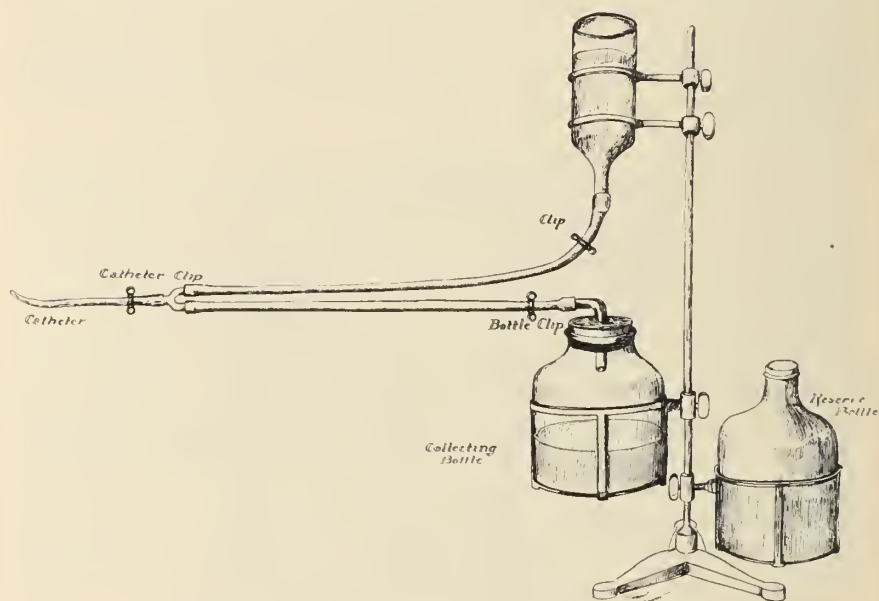
FIG. 3. St. Mark's Hospital Retained Catheter Apparatus

Directly after the urine has been released, the tubing must be washed through with antiseptic and kept full of antiseptic.   To *release urine* open bottle clip and catheter clip and urine will flow into collecting bottle.   To *wash out the tubing*, first see that catheter clip is closed, then open antiseptic clip and bottle clip.   Antiseptic will run from reservoir to Y-shaped junction and back to collecting bottle. When tubing is full of antiseptic close both clips.   To *irrigate the bladder*, first fill up the antiseptic reservoir with acriflavine solution from the reserve bottle.   Raise the reservoir a few inches above the bed and notice level of antiseptic.   Open antiseptic clip and catheter clip and let fluid run into bladder.   As soon as the patient begins to feel discomfort, close antiseptic clip and open bottle clip, and fluid from the bladder will run into collecting bottle.   Wash out tubing.

in these patients treated by retention catheterization (the specimens were not centrifugalized) disclosed that the urine was negative in eight, contained a few white blood cells in nine, and many white blood cells and an occasional red blood cell in four.   Pus was present in three cases.

The catheter was permanently removed on the third day in two patients, on the fourth day in seven, on the fifth day in two, on the sixth day in four, on the seventh day in three, on the eighth day in two patients. It was retained in one patient for eighteen days.   In the two cases treated

by intermittent catheterization, it was continued for eleven days in one, and for thirty-six days in the other. In the first, a frank purulent cystitis developed, and in the second, who died a year later from the effects of arteriosclerosis of the kidneys, the autopsy disclosed a chronic cystitis.

Eighteen of these patients have been followed from eight months to three years. There was only one who complained of a troublesome cystitis which eventually was controlled after ten months of bladder irrigations. However, none of these patients experienced any difficulty with micturition.

It is granted that the number of cases in this series is so small that it is extremely difficult to draw any definite conclusions. It would seem, however, that the urinary retention, while universally present following major proctectomy, is best treated by the indwelling catheter along the lines suggested by Duke. Although a case of gangrenous cystitis resulting in death occurred in this series, the Duke method could not be held culpable in this diabetic patient because the absence or mildness of the cystitis in eighty-five per cent of the cases, and the absence of vesical dysfunction after removal of the catheter in all cases, definitely commend this method.

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THE TREATMENT OF VESICOVAGINAL AND RECTOVAGINAL FISTULAE

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The successful closure of vesicovaginal and rectovaginal fistulae depends upon numerous factors. Chief among these are the nature of the injury, its etiology, the experience and skill of the operator, and to some degree the postoperative treatment.

In summing up the treatment of thirty* cases of vesicovaginal fistula and ten** of rectovaginal fistula, cared for by myself in the course of thirty-one years in the gynecological ward and private pavilion of The Mount Sinai Hospital, certain clear cut features become apparent. Vesicovaginal and rectovaginal fistulae, however, must be discussed separately, although in many ways the conditions, as well as the treatment, resemble each other.

VESICOVAGINAL FISTULA

Previous unsuccessful operations. It is easiest to cure fistulae at the first operation. Each subsequent operation increases the amount of scar tissue encountered, reduces the mobility of the structures and impairs the vascular supply. Therefore the responsibility of performing an operation for vesicovaginal fistula is great and this intervention should not be undertaken lightly, especially by the inexperienced or occasional gynecologist.

Of the thirty patients, twelve had been operated upon from one to six times by others, previous to coming under my care. These cases all proved difficult, as during the preceding interventions much tissue had been lost and the sphincteric structures either sacrificed or destroyed. In consequence, in contradistinction to other groups, only six were cured, five were improved to a considerable degree and one remained unimproved. The sole exceptions to the cardinal rule of attempting to close a vesicovaginal fistula at the first operation are those complicated cases where the great difficulty of approach, the dense scar tissue and fixation, as well as complete destruction of the vesical neck and sphincter, oblige one to perform the repair in stages.

Spontaneous Closure. Recent fistulae, both those due to intrapartum

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* Sixteen of these cases of vesicovaginal fistulae were analyzed in a paper appearing in 1917 (1).

** Three of these cases were reported in 1932 (2).

trauma or resulting from operation or external injury, may close spontaneously if the bladder is put at rest at once, in the fully contracted state by means of a permanent catheter retained at least fourteen days.

In this series three closures occurred spontaneously. Two of these patients had developed fistulae after abdominal hysterectomy for cancer of the cervix, another from a long and difficult labor. Small openings, situated high, are most apt to heal.

If, in the course of a gynecological operation, the bladder is injured or must be resected, immediate repair in two or three layers should be practiced and a retention catheter employed. Then fistulous development is most unusual. I have no statistics available, but, with impunity, have repeatedly resected portions of the bladder transperitoneally in the removal of cancer, sutured, peritonealized and closed without drainage, except the permanent catheter introduced through the urethra. Twice in the course of operations for cystocele, and once during a vaginal hysterectomy, I have opened the bladder, and immediately repaired the rent without complication or sequel.

Transurethral Fulguration. Minute, especially inaccessible, residual fistulae, may remain after closure of large defects, and, from the patient's point of view, entirely defeat the success of operation.

As I pointed out in 1917 (1), such small fistulae may be closed by one or more intravesical fulgurations. This small intervention may be performed on the ambulant patient without even local anesthesia, through a water cystoscope, with the apparatus and by the method developed by Beer (3) for bladder papillomata. Two patients were cured by fulguration alone; in three, fulguration some weeks or months after operation closed residual fistulae (three in one patient).

Success depends upon the size of the vesical opening. No fistula larger than twice the diameter of the normal ureter opening can be closed. If, in addition, the bladder mucosa is succulent and hypertrophic in the neighborhood of the defect and the vesicovaginal septum thick, success should be assured.

Mobilization of the Bladder. In principle, full mobilization of the bladder promises the most certain hope of cure. This may be practiced from below, as in the operation for cystocele, or from above, transperitoneally. Unfortunately, the presence of contractures, scars and indurations prevent the routine use of this method.

Full mobilization was practiced in eight cases, twice from above with preliminary transcervical hysterectomy and six times per vaginam.

This technic is particularly successful when the fistulae are close to and adherent to the cervix or uterus (Figs. 1 and 2). During the course of the procedure, it may be necessary, in order to obtain hemostasis, to ligate one or both uterine arteries close to the uterus. This does not impair the vitality of the womb. The technic is rarely applicable in those cases

in which the fistula is more peripheral, particularly those fistulae densely adherent to the posterior surface of the symphysis pubis.

In high fistulae occurring after complete hysterectomy, either vaginal or abdominal, and especially those which have resisted previous operation, a method described by Kelly many years ago, and too often forgotten, can be applied. After the fistula has been visualized, its edges circumscribed, and the vaginal mucosa fully mobilized, it may be of great advan-

FIG. 1.   FIG. 2.

FIG. 1. Vesico-cervico-vaginal fistula

The vesical fistula is seen to open directly on the portio vaginalis and into the lower part of the lacerated cervical canal.
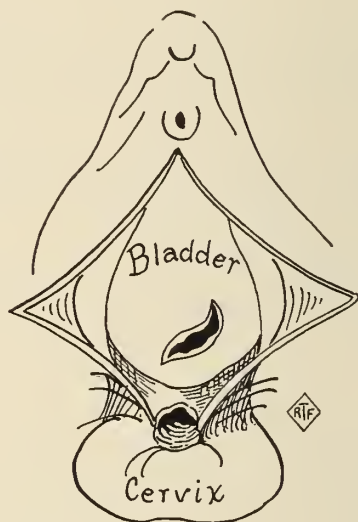
FIG. 2. Same case as in figure one

Shown after reflexion of anterior vaginal wall and mobilization of the bladder, as in cystocele operation. This frees the vesical defect completely and exposes the injured cervical canal. Bladder and cervix are sutured separately, and cystocele operation performed.

tage to open the partly obliterated cul-de-sac and boldly enter the peritoneal cavity. It will then be found that the higher portions of the bladder readily can be drawn into the vagina (Fig. 3), permitting transverse suture of the bladder rent without tension. A small piece of rubber dam introduced into the cul-de-sac will insure against prolapse of the intestine and infection, an indwelling catheter draining the bladder.

Six cases were treated by mobilization of the bladder. All of these

were cured, one, however, subsequently requiring the closure of a small residual fistula by the Sims' technic.

Flap Splitting. The most universally applicable technic is that of flap splitting in which the fistula is visualized and the vaginal mucosa separated for a distance of one-half to one centimeter around the defect. The bladder opening is then closed by two layers of fine chromic sutures, neither of them including the vesical mucosa (Fig. 4). Should difficulty be encountered in inverting the bladder mucosa, interrupted sutures may be passed around the circumference of the fistula, taking only the mucosa, and then, by means of a probe, drawn through the urethra. When drawn tight, the bladder mucosa is inverted making it easy to suture the muscle and fascia. After this step has been completed, the untied sutures, which
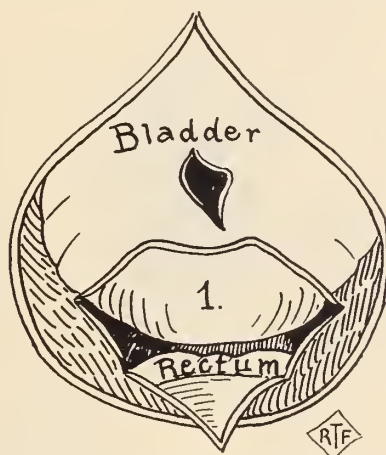
FIG. 3. Mobilization of high vesicovaginal fistula occurring after vaginal hysterectomy

The culdesac has been opened, the base of the bladder pulled down into the vagina, thus removing all tension. 1. Intraperitoneal part of bladder.

have been drawn through the urethra are removed through the meatus by pulling on one end of the loop. After the vesical suture, the mucous membrane of the vagina is united. Should the vaginal tissues be too rigid or too scant to permit of complete coverage of the bladder, a pedicle flap may be made from the labium minus in order to close the vaginal defect entirely. Not infrequently the flap method advantageously may be combined with partial mobilization.

As Halban (4) recently restated in an article on vesicovaginal fistula, failure frequently depends on lack of boldness in mobilizing the tissues, irrespective of scars and contractures. The principle of wide mobilization, however, does not apply as much to cases operated on repeatedly as to the early cases as yet undamaged by unsuccessful attempts at repair.

In my series, eleven cases were treated by the flap splitting method. Eight were cured, two were improved (in both of these, sphincter defects were present), and one was cured by other technics at a later session.

Sims' Technic. The original technic of Sims, consisting of coning out of the fistula, and approximation of the raw surfaces broadly by silver wire suture, still proves of great value under certain conditions. When the fistula is extremely inaccessible and tightly fixed by scar tissue, I know of no method which is simpler and more promising than this technic (Fig. 5). It was employed in two cases with cure. In the one case, I
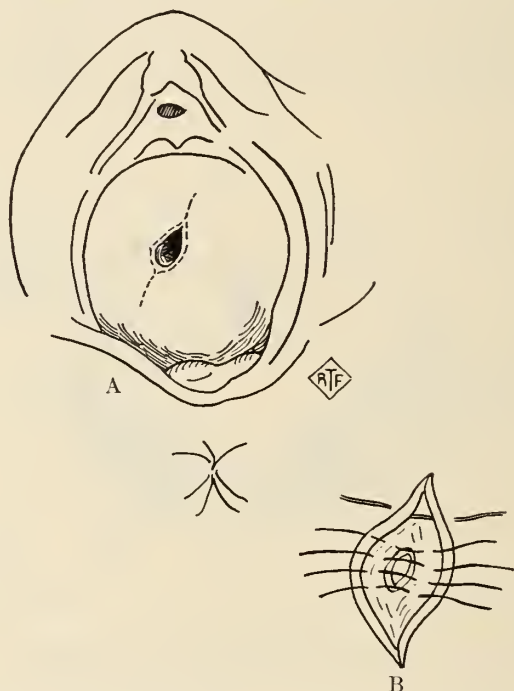
Fig. 4. Vesicovaginal fistula. Flap splitting technic

A. Broken line shows vaginal incision.

B. Vaginal mucosa reflected, exposing bladder musculature and fistula. Four bladder sutures shown; one vaginal suture.

employed alternately flap splitting and Sims. The final sixth operation was performed by the Sims' method (vida infra).

Defects with Absence of Urethra or Destruction of the Vesical Sphincter. My ideas on the treatment of these cases have changed greatly in the course of the years. In my earlier activities I carried out difficult reconstructive flap plastics first for restoration of the urethra, then closure of the large defects, and finally junction of the newly established urethra and bladder. Patience and repeated operations in several cases resulted in the formation of a continuous bladder and urethra, but in no instance was control

fully re-established.   In two of the five cases, a fair degree of control was obtained by the additional use of pressure pessaries.   These unfortunate patients were subjected to from three to five or more operations but not a single one can be classed as a perfect result.   Today even more complicated procedures are advised by others.

In my opinion the best way to treat such patients, if a large defect exists in the vesicovaginal septum through which the bladder fundus prolapses, is to reduce this opening by mobilization and suture, to approximately one-half centimeter in diameter and then subject the patient to implanta- . tion of the ureters into the sigmoid.   I am well aware that this procedure is dangerous and involves a mortality of 6 to 10 per cent, but, if successful, the patient is fully restored to health and activity.   Of the five cases in
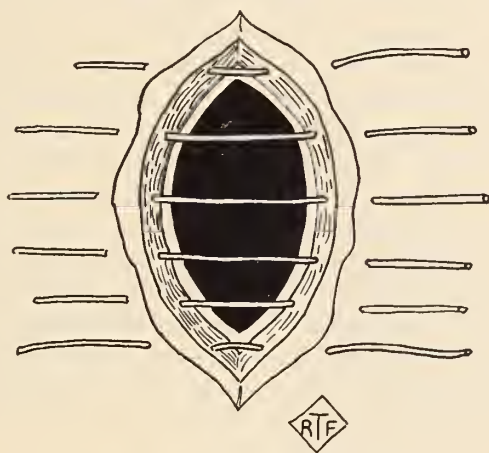
Fig. 5. Sims' technic

Fistula coned out.   Silver wire sutures in place taking all layers except the mucosa of the bladder which inverts if the sutures have been properly inserted.

question, I have in the last few years referred two to Dr. Edwin Beer for this procedure.

Radium Fistulae.   Vesicovaginal fistulae resulting from radiation, particularly radium locally applied to carcinoma of the anterior wall of the vagina, have not responded to repair.

A case in point is that of C. F. in whom a carcinoma of the cervix circularly involving the vagina, was treated in June of 1931 with large doses of radium and X-ray.   In December 1933 this patient presented herself to me with a large vesicovaginal fistula extending from the vesico-urethral junction to the completely involuted and scarry cervix.   The bladder fundus, red, irritated and hypertrophic, presented through the defect.   As this patient showed no signs of recurrence in January 1934, a readily performed mobilization and suture in layers was done.   The

vaginal mucosa was brought together with silver wire. Not the slightest sign of union was noted. Another attempt to close the fistula was made in December of 1936. A complete and easy operation was performed. No healing whatever took place. This patient was later referred to Dr. Beer for transplantation of the ureters.

The same lack of healing occurs likewise in rectovaginal fistulae due to radium, if situated in the lower two-thirds of the vagina.

Preoperative Treatment. Many of the cases suffering from vesicovaginal fistulae present themselves in a desolate condition, the thighs, vulva and vagina being excoriated, covered with incrustations, the urine showing the effects of cystitis.

Preliminary treatment may be given at home to those who can receive proper care there, or in the hospital for several weeks. Hot sitz baths, bland irrigations of the vagina, and application of vaseline gauze to excoriated areas, clean up the local condition in the majority of cases. In the presence of excoriations, if the urine is acid, alkalinization may be of service. A ketonic diet in some cases clears up the excoriations rapidly but in two instances I have had the impression that failure of the repair was due to this measure. Therefore I prefer to operate in the presence of an alkaline urine and in no circumstances do I give urotropin either before operation or during immediate postoperative treatment, as this drug appears to favor too early absorption of the catgut sutures.

Sometimes a vaginal operation is rendered difficult by the presence of scars which narrow and distort the vagina. Under these conditions, mercury colpeurysis, performed once a day over a period of several weeks, may not only soften the scars to an amazing degree, but likewise enlarge the vagina and thus facilitate approach.

Where the bladder is found extremely contracted because of the long persistence of vesicovaginal fistula, preliminary bladder distension is of great service. This usually may be performed with ease by arming a small rubber catheter, 12 to 15 French, with a finger cot or rubber condom fastened in place by a silk ligature, and introducing this home-made instrument within the bladder. The viscus is gradually distended by introducing increasing amounts of sterile water into the bag, left in situ for five to fifteen minutes. With this treatment a distension of 50 or 75 c.c. is obtained within one to two weeks.

Postoperative Treatment. The main safeguard is the permanent catheter introduced just beyond the junction of the urethra and bladder. My instructions are that the resident staff must be called at once if the urine flow through the catheter ceases. To insure adequate supervision, the drainage bottle is graduated and inspected every half hour, careful note of the amount present being recorded.

Incrustation and consequent closure of the catheter is best prevented by washing out the bladder twice daily with sterile water, never using

more than 10 c. c. at a time, and making sure that this amount is recovered
at once.   In some patients the catheter must be changed because of
closure; the re-introduction must be done delicately by experienced hands.
I have found no advantage accruing from the prone posture advised by
Miller (5).   The bowels of the patients operated on for vesicovaginal
fistula, are constipated from eight to ten days because the straining at
stool places such tension on the approximated tissue that tearing of the
suture line may result if early catharsis is induced.

One patient left the hospital on the fourteenth day fully cured.   That
night coitus was indulged in and the fistula re-opened, requiring re-opera-
tion.   This time silver wire sutures were left in situ for six weeks.

Stone Formation After Operation.   In two instances, both of which were
mentioned in my 1917 communication, collar button stones formed in
diverticula resulting from operation.   The one was operated transvesically
from above, the diverticulum being obliterated by flap resection.   The
other was cured by free incision of the vesicovaginal septum and oblitera-
tion of the diverticulum from below with immediate resuture.   Such oc-
currences may be forestalled by mobilization of the bladder at the primary
repair.

In several instances sutures used in the closure worked through into
the bladder lumen and there produced soft stone formation.   The sutures
were removed transurethrally through a cystoscope and the granulating
areas cauterized.   In one patient a Christmas tree-like soft calculus re-
formed repeatedly at the site of the previously closed vesicovaginal fistula.
The condition was cured by thorough but superficial fulguration of this
area.

RECTOVAGINAL FISTULAE

Spontaneous Closure.   Of ten cases, two healed spontaneously.   Both
of these were situated high behind the cervix and probably communicated
with the lower portion of the sigmoid flexure.   The one was due to radium
application to the cervix for carcinoma.   This patient received X-ray
treatment in January 1930 for intracervical carcinoma, and radium treat-
ment in March of the same year.   A rectovaginal fistula developed high
behind the cervix some months later, persisted for over a year and then
spontaneously closed.   The patient still shows no signs of recurrence in
June of 1937.

The second patient, a young woman, suffered from bilateral pyosalpinx,
which produced recurrent attacks responding to no form of therapy over
the period of one and one-half years.   The inflammation followed a curet-
tage, though gonococci were never demonstrated.   The extremely difficult
operation consisted of supravaginal hysterectomy and bilateral oophorec-
tomy.   The patient was drained from above and also below through the
cored-out cervix.   On removal of this drainage, eight days after operation,

fecal leakage through the vagina was noted and persisted for eighteen days. The fistula has remained permanently closed and the patient is in good health.

Post Partum Rectovaginal Fistulae. Two cases in which post partum rectovaginal fistulae developed soon after labor, were operated upon. In the third, the fistula was residual after an operation for third degree tear. All three were cured operatively, the last requiring two interventions.

Rectovaginal Fistulae from Inflammation. I have seen three of these cases, two resulting from well marked chronic colitis, the other from an abscess in the perineal septum, seemingly due to this same etiology. The one resulting from the perineal abscess was cured by two operations. In neither of the active colitis cases has a cure been obtained. Both of them showed complicated sinuses. Because of the colitic condition, operation was not considered advisable, and repeated fulgurations were resorted to. While these reduced the discharge and the local discomfort, cure has not resulted.

Traumatic Cases. One patient fell from a chair which broke, the chair rung perforating the rectum and vagina. The resulting granulating wound was allowed to heal. A small rectovaginal sinus persisted and was readily closed by fulguration.

The other case, a child, when first seen six years of age, fell through a skylight. The resulting injuries consisted of multiple perforations of the intestine, recto- and vesicovaginal fistulae. The intestinal repair was performed at once. The child recovered from the intestinal injuries and later at the same hospital, two attempts to close the vesicovaginal fistula were made without success.

When first seen by me the child was in a miserable condition from the cloacal discharges. The parts were very small; much scar tissue had formed. Six operations for vesicovaginal fistulae, three by flap splitting, three by the Sims' method, were done over a period of two and one-half years, with complete cure of the vesicovaginal defect. Some months later the rectovaginal fistula was cured by one operation, the child now being in perfect health.

Operative Technic for Rectovaginal Fistulae. An attempt to favor spontaneous closure in recent post partum rectovaginal fistulae may be made by constipating the patient for twelve to fourteen days. Unless the fistula is very high behind the cervix, little hope of success can be entertained.

No operation should be undertaken before all the granulations have disappeared and the rectal and vaginal mucosal edges have united.

The technic employed was uniform with only minor variations and every case operated upon was cured eventually. A simple flap splitting, with sufficient mobilization of the rectum to permit approximation without tension, was employed. Through and through sutures through the rectal mucosa, with the knots in the rectal lumen and the suture pulled out

through the rectum, are best. The rectal fascia is next united by fine continuous chromic gut. Interrupted sutures of the vaginal mucosa are then inserted. If the perineum is deficient it may be built up at the same session. The patient is constipated for at least nine days. After the fifth day a low residue diet may be given. The bowels are moved by giving mineral oil over two or three days and then adding small doses of milk of magnesia to the oil. Finally a small oil retention enema is put into the rectum; next morning a saline cathartic is given to insure a good movement.

From this casuistic of vesico- and rectovaginal fistulae, it is apparent that each case requires individual study. The method of approach— vaginal, transperitoneal or transvesical—must be selected with judgement. A definite plan must be laid out and followed. Under no circumstances should tissue be sacrificed. This warning applies particularly to the fascial and sphincteric structures.

Preoperative preparation, for days or weeks, should not be neglected. Vaginal approach may be facilitated by colpeurysis, the Schuchardt incision and traction by the Gerrahty retractor passed through the fistulous opening.

With few exceptions chromic gut should be used for suture. In the Sims' technic silver wire is employed.

Postoperatively, minute care, prolonged rest, sufficient fluids and no bowel movement for eight to ten days, are recommended.

These lesions tax the fortitude of the patient, as well as the patience of the surgeon, to the utmost, but, by persistence, the vast majority of these unfortunates are eventually cured.

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AN UNUSUAL TYPE OF CONGENITAL HERNIA

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The anatomical features presented by the following case are of such unusual interest and rarity as to warrant a detailed report.

CASE REPORT

History (Adm. 362254). A male infant of 15 months, was admitted to the service of Dr. Richard Lewisohn on February 2, 1934, and discharged on February 22, 1934. His parents stated that since birth they had noted a mass in the infant's left groin. This had gradually increased in size. They consulted a physician who advised a truss which was worn for two months without effect. The inguinal mass was always easily reducible.

Examination. The patient was a robust male infant weighing twenty-two and a half pounds. The general examination was negative except for the local surgical condition. In the left part of the scrotum was a large oval mass which extended up into the inguinal region. It was easily reducible into the abdomen, but yielded an impulse when the infant cried. It transilluminated light. The left testis could not be felt. A diagnosis of left congenital hernia was made.

Operation. It was performed on February 5, 1934. An inguinal incision was made. The cremaster muscle was found to be unusually hypertrophied. Occupying the inguinal canal was a large hernial sac which emerged from the internal ring. It was isolated and dissected free from the surrounding tissue and cord structures after considerable difficulty. It was not of the congenital type. The testis was found to be situated in the normal position in the scrotum. When opened, the sac was seen to consist of two compartments, each segment of the oblique variety. Separating the two, was a diaphragm about one-sixteenth of an inch in thickness and lined with peritoneum on both surfaces. The mesial sac contained a sliding hernia of the sigmoid colon; the external sac, a sliding hernia of the small bowel. The mesentery of each loop of bowel seemed to be part of the diaphragm separating the two sacs. The examining finger could trace the diaphragm for an indeterminate distance within the abdomen. Its termination intra-peritoneally could not be located. The external hernial compartment was closed by a running stitch, whereas the internal sac was closed by the Hotchkiss method, reconstructing the mesentery of the sigmoid. Repair of the inguinal canal after the method of Ferguson completed the operation.

Convalescence was uneventful and the wound healed by primary union.

Follow-Up. The patient was last seen one year after discharge from the hospital. At that time there was no evidence of recurrence.

COMMENT

Study of the accompanying diagrammatic sketch of the findings at operation will disclose the unusual features of this case. The entire hernial sac with its enclosed dividing diaphragm was oblique in position,
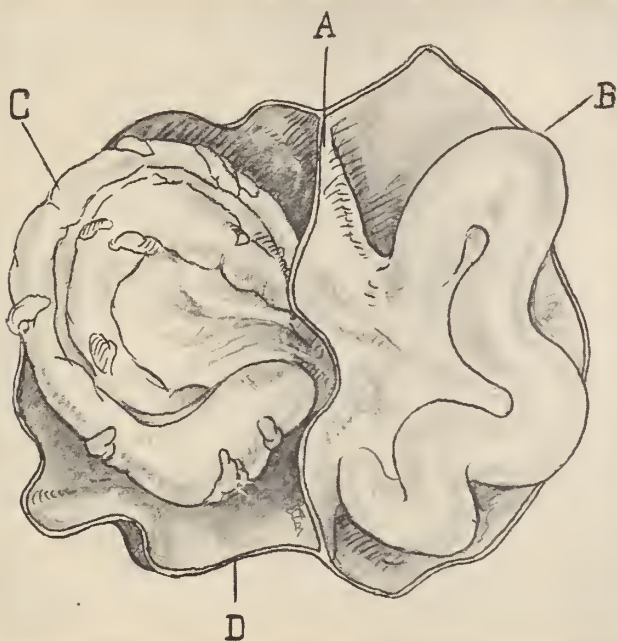
FIG. 1. Diagrammatic sketch of the findings at operation. The excess of the hernial sac has been excised. "A" represents the diaphragm dividing the sac into two components. In the external compartment is a sliding hernia of the small bowel "B". The internal compartment contains a sliding hernia of the sigmoid "C". The mesentery of each loop forms an integral part of the dividing diaphragm. The cut edge of the hernial sac is indicated at "D".

i.e., the neck of the sac emerged external to the deep epigastric vessels. The diaphragm, which was covered by peritoneum on both surfaces except at the point of attachment of small bowel on one side and sigmoid colon on the other, divided the sac into two compartments. The external compartment contained a sliding hernia of small bowel. The mesial compartment presented a sliding hernia of the sigmoid. The mesentery of each loop of bowel seemed to be part of the diaphragm which divided the hernial sac into two components. This explains why the contents of the hernial sac were easily reducible before operation.

In explanation of this peculiar anomaly, two possible mechanisms come to mind. It may be argued that the wearing of an ill-fitting truss could set up an inflammatory reaction within the sac and produce the bizarre picture disclosed at operation. In favor of such a thesis is the finding of extensive scarring in the inguinal canal which made the dissection of the sac from the surrounding structures somewhat difficult. However, the entire absence of adhesions within the sac and the almost anatomical precision of the attachment of both loops of bowel to the diaphragm are important points against such an hypothesis. An alternative explanation of the findings rests on embryological grounds. The absence of inflammatory adhesions within the sac and the age of the patient support such a contention. However, I can find no embryological explanation for the anomaly nor can I find a case report of a similar sort in the available literature.

Attention is called to an extremely useful and simple method of dealing with sliding hernia, a method which was utilized in closing the mesial compartment of this hernial sac. It would appear from the literature that it was first described by Henversyn in 1893, but it was popularized by Hotchkiss in 1909 and is now known as the Hotchkiss method. It consists of a reconstruction of the mesentery without separating the bowel from its attachment. The suture, which is begun at the point of attachment of the bowel, is carried around the cut edge of the hernial sac. With each succeeding stitch, the bowel inverts more and more until the entire mass of bowel and sac invaginates into the abdomen.

THECA CELL TUMORS

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There is still considerable scepticism expressed as to the existence of a separate neoplastic entity that can be classified as arising from the unused theca cells in the ovarian parenchyma. Most investigators believe that the tumors described as theca cell tumors are really granulosa cell growths. In the literature at present Loeffler and Priesel, Melnick and Kantor, Geist and Spielman, Geist and also Hubert have described and illustrated neoplasms that differ so definitely from the granulosa cell tumor in morphology and in some striking clinical features, that it seems to the author conclusively established that there exists a group of new growths which arise from the unused theca cells of the parenchyma. The ovarian parenchyma is composed of many cell types. Among them are granulosa cell forerunners and theca cell forerunners. As follicles develop, stimulated by the growth of an ovum, these cells become the mature granulosa cells and theca cells of the follicle. Some remain unused. Evidence is accumulating to substantiate the fact that these two cell types have many features in common. However, other evidence supports the fact that there are also definite variations in their characteristics. Both cell types store or form lipoids and they both store or produce an estrogenic hormone. Zondek showed that the theca interna cells contain an estrogenic hormone in greater amount than the granulosa cells. The lipoid also differs in the two types of cells. In the granulosa it is scant in amount being present in large quantities only when the cells are undergoing degeneration, while in the theca cells the lipoid is much greater in quantity in the normal functioning cell. In addition, in the granulosa cells the lipoid is mainly phospholipid and neutral fat, whereas in the theca it is mainly cholesterol or the cholesterol esters. Both cell types seem to stimulate connective tissue growth, but here too the stimulating effect seems a more marked characteristic of the theca cell. It has been noted that under conditions as yet not clearly understood the parenchymal theca interna cells are stimulated and increase in number, even becoming luteinized (Fig. 1). This condition may be associated with definite clinical findings. It is natural to suppose that the immature granulosa cells and theca cells may give rise to tumors and also natural to expect that there would be morphological if not clinical variations between the two types. The author in collaboration with Spielman and Gaines has published a total

of seventeen tumors that they believe fall into the group of theca cell tumors.

The theca cell tumors vary from a type resembling a fibroma, being spindle-cell in character but containing fat (Figs. 2 and 3), to the typical cases with large epithelioid fat containing cells separated by masses of hyalinized connective tissue plaques (Fig. 4). The gross and histological pictures also vary somewhat. The tumors usually are solid, hard, somewhat nodular growths that may reach the size of an adult's head. They suggest fibromas in consistency and appearance but, unlike fibromas, are not accompanied by ascites except in the rare malignant type. On the

FIG. 1   FIG. 2

FIG. 1. Luteinized parenchymal theca cells
FIG. 2. Fibroma-like theca cell type
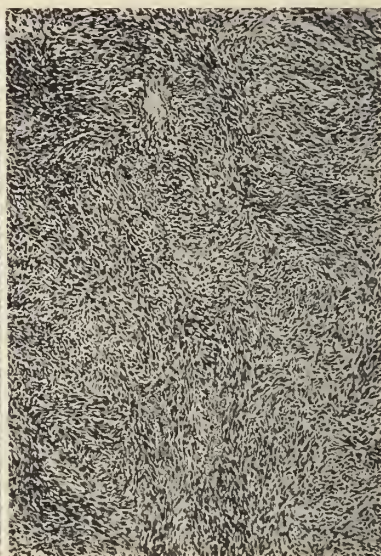
other hand, the tumor may be represented by a large degenerated thick wall cyst. Not uncommonly it may be associated with other ovarian neoplasms such as dermoids or multilocular serous cysts. On section the cut surface is distinctive both in the solid and cystic variety. The cut section of the solid tumors or the thickened wall of the cystic tumor is usually yellowish white, the color being due to the presence of varying sized yellow cellular islands separated by fine or coarse hyaline connective tissue bundles (Fig. 5). The connective tissue may be so massive in amount that the cut surface of the tumor may exhibit white hyaline areas containing only tiny pin head sized islands of light yellow color, or are studded with a few or many large isolated nodules of deep yellow color (Fig. 6). Small hemorrhagic areas and at times degenerative cysts,
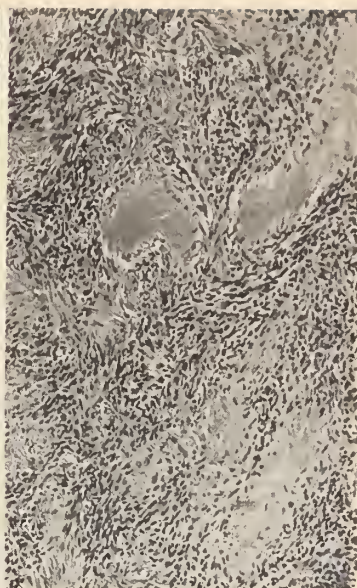
FIG. 3   FIG. 4

FIG. 3. Fibroma-like theca cell type
FIG. 4. Typical theca cell

FIG. 5   FIG. 6

FIG. 5. Typical theca cell type (Gross)
FIG. 6. Cell islands with massive connective tissue

which may coalesce, are found. Histologically the tumors in the main present a picture varying decidedly from that of the granulosa cell tumors. The yellow islands are composed of plump spindle- or polygonal cells

with a central or at times an eccentric elongated or irregular nucleus, dark staining and rich in chromatin (Fig. 7). The cell protoplasm is vacuolated and contains fat. To a slight extent fat is present in the interstitial tissue. Blood vessels are present as fine capillaries and as large vessels in the connective tissue capsules and at the periphery of the cellular islands. Pigment granules (lipochrome) are present in the cells and in the vessel endothelium at times. The epithelioid cell islands may be few or many in number, the cells containing fat (Fig. 8).

The connective tissue bundles are hyaline to a great extent and frequently large hyaline plaques with radiating fibrils extending into the more cellular zones and surrounding the individual cells are found (Fig. 4).
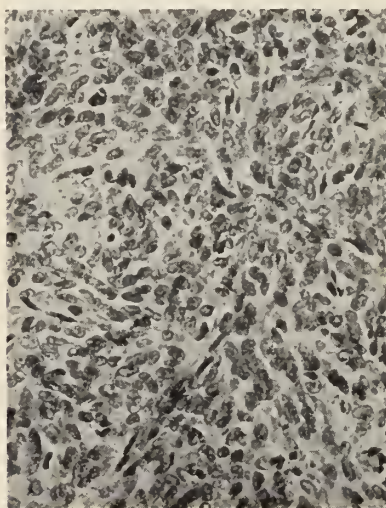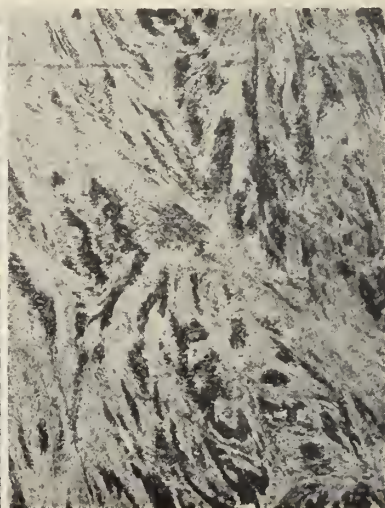
Fig. 7   Fig. 8

Fig. 7. Epithelioid cells of theca cell tumor
Fig. 8. Fat in cellular islands

The fibrous tissue bundles and plaques vary in size, density and structure. They may be very fine, composed of but a few fibrils or so massive as to represent the greater part of the tumor (Fig. 6). They may be composed of a few connective tissue bundles or large masses of hyaline tissue. Connective tissue cells may be scant in number while in the fibrillar meshes isolated cells resembling the true tumor cells and containing fat are found. The connective tissue bundles run in a criss-cross network surrounding the cellular areas while fine fibrils may encircle cell groups or individual cells.

The cysts as previously mentioned are probably degenerative in origin. The walls may be smooth or shaggy. The contents are a yellowish clear or turbid fluid containing cholesterol crystals, fat droplets, cellular débris and possibly an estrogenic hormone. There is no definite lining, though

occasionally a row of flattened endothelial like cells is found in scattered areas.

Clinical study as well as microchemical and polariscopic investigation demonstrate that these tumors contain a non-degenerative type of fat. It is limited almost entirely to the cellular elements (Fig. 8).

In one case Geist and Spielman reported the presence of an estrogenic hormone. When fat is scant in amount and the tumor more fibromatous in nature, the signs of estrogenic hormone stimulation, such as bleeding or enlargement of the uterus and breasts, are absent.

Clinically these tumors commonly occur as unilateral growths in women past the menopause. They are associated with uterine bleeding and often signs of estrogenic activity such as enlargement of the uterus, cystic hyperplasia of the endometrium and breasts. After removal of the tumors the symptoms and signs usually regress. While the tumors are usually benign, Loeffler and Priesel, Geist and Gaines, and Hubert have each reported a malignant type with ascites and metastases.

It is evident that a decided difference exists between the granulosa cell tumor and the theca cell tumor. It is evident that with two separate types of cells in the parenchyma of the ovary two distinct types of tumors may develop. The gross appearance of the two tumor types varies; the theca cell tumor is a hard, fibrous yellow growth whereas the granulosa cell tumor is a more cellular, medullary softer whiter neoplasm. Nowhere in the theca cell tumor does one find areas that grossly or microscopically resemble the morphology or pattern of the typical granulosa cell tumor. Chemically the tumor differs somewhat in so far as the lipoid distribution differs. In the theca cell tumor the fat is usually more abundant and consists mainly of cholesterol or cholesterol ester.

While the clinical syndrome is similar, as is natural in tumors arising from cells having such closely allied biological properties, still there are some slight differences. No theca cell tumors have been found in children, whereas Klaften has reported that 8.9 per cent of granulosa cell tumors occur before puberty. Furthermore while granulosa cell tumors occur in 48.8 per cent after the menopause the theca cell tumors occur in 83 per cent post menopausal. It is because of these differences in histology, chemistry and the clinic that we feel we are dealing with two separate entities, one arising from the granulosa cell forerunner in the ovarian parenchyma and the other from the theca cell forerunner.

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INVOLVEMENT OF THE INFERIOR VENA CAVA IN RENAL NEOPLASMS

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In a series of one hundred and eighty-seven malignant neoplasms of the kidney in adults, eleven cases showed extension of the tumor into the inferior vena cava. Most of these were recognized by the surgeon at the time of operation, but one case was unsuspected until post mortem examination. This type of complication presents a number of features of considerable interest. They do not all terminate fatally within a short time; occasionally, a case is amenable to surgical intervention.

Pleasants (1) in 1911 collected three hundred and fourteen cases of inferior vena cava obstruction. Twenty-eight of these were due to renal neoplasms. Simpson (2) in 1924 added six more cases to the latter group. Since then a number of isolated references are to be found in the literature. In Bothe's (3) series of nineteen autopsied cases of hypernephroma, two showed involvement of the vena cava (cases 4 and 9) and both arose from the left kidney. Kümmel (4) extracted a thrombus projecting from the renal vein into the inferior vena cava and the patient was still well after fourteen years. Polayes and Taft (5) cite a case in which the cava was filled with tumor thrombus from the iliac veins to the right auricle. This was due to an extension through the left renal vein stump in a patient who had had a nephrectomy for hypernephroma eight months previously. They found fourteen similar reports in the literature of cases in which the thrombus extended into the heart. Walters and Priestly (6) encountered one case in which the vena cava was opened and the thrombus was extracted, and another in which a projecting thrombus in the cava could be milked back into the renal vein. Ljunggren (7), Beneke (8) and others have also contributed reports of cases with caval involvement.

PATHOLOGY

Although it is well known that hypernephromata frequently involve the renal veins, other types of tumors have been reported to have invaded the vena cava. The variety includes; carcinoma, adenocarcinoma, squamous cell carcinoma, papillary carcinoma, teratoma, myxosarcoma, endothelioma and lymphosarcoma.

Considering the fact that the right renal vein is shorter than the left, the vena cava may be expected to be involved less often with left-sided

tumors than with right. Thus in Simpson's series of thirty-four cases, extension to the cava was due to left renal neoplasms in eleven cases.

The extent of involvement varies from a small projecting bud into the cava to complete occlusion of the vessel from the femoral veins, through the right auricle and into the ventricle. These thrombi are grayish or yellowish in color, resemble the main kidney tumor and microscopically are infiltrated by tumor cells. These cells are treated as foreign bodies and are usually enmeshed in a mural thrombus. Since this forms an excellent medium for the propagation of tumor cells, a progressively advancing thrombosis results. The plug grows upward in the direction of the blood flow, but downward extension also occurs, especially after the lumen is completely occluded. Pleasants states that these thrombi may form a complete mould of the vessel without actual invasion of the vessel wall by tumor cells. Bothe (3) quotes Wright's (9) statement that the tumor thrombi are separated in most instances from the vessel wall by fibrin, red and white cells; and that the tumor cells growing within the lumen of the vessel may have no connection with the vein wall.

As one can surmise, these tumor thrombi may be soft and result in emboli. This was definitely shown in the post mortem examinations by Judd and Scholl (10), Polayes and Taft, Jacobson and Goodpasture (11), Simpson and others. On the other hand, there is evidence to show that this is not always true, despite the statement by Bumpus (12) that "it is unlikely for a hypernephroma to be in the vena cava without resulting in metastases". French (13) reported the post mortem findings in a patient who suffered from a left renal neoplasm which extended through the renal vein, and into the inferior vena cava and right auricle. The thrombus was infiltrated by tumor cells throughout. There were no pulmonary emboli, and no evidences of either edema or collateral venous circulation. Mayo (14) removed a tumor thrombus from the vena cava and the patient lived over five years. Kümmel's patient lived over fourteen years. Beneke reported a case of left renal neoplasm that ruptured into the cava and no metastases resulted. Ljunggren had a similar case. The latter also reported a case in which a renal neoplasm with extension into the cava was removed. This patient died five years and eleven months later, and a post mortem examination revealed no evidences of metastases, local recurrence or trace of tumor in the cava. Thierry's (15) patient is an unusual example. He removed a Grawitz tumor in 1906 but did not remove the extension into the vena cava. This patient lived for eleven years, although one year before his death, enlargement of the liver, ascites and dilated superficial veins developed. These are typical evidences of caval obstruction.

SYMPTOMS AND SIGNS

The fact that most of the cases of vena cava obstruction were diagnosed only post mortem, speaks for the few manifestations that these patients

may exhibit clinically. Pleasants considers the symptoms and signs under two headings: (1) those due to the mechanical obstruction per se; and (2) those due to the original source producing the caval involvement.

The former depend upon the position, extent, rapidity and completeness of the occlusion. Evidences of caval thrombosis may be present without any of the usual symptomatology of kidney tumor. Experimental ligation of the cava below the level of the renal veins may not result in any signs of caval obstruction. Above the renal veins, acute occlusions are fatal. Slow blockade of the vena cava allows for the development of an adequate

FIG. 1. Hypernephroma of the right kidney. Extension into the right renal vein and inferior vena cava. Obliterating thrombus of the inferior vena cava, left renal and ovarian veins.

circulation. There are several paths for the return of blood to the heart in obstruction of the inferior vena cava. The more important are the superficial veins of the skin, the lumbar azygos channel, the arcaded vertebral plexus, the inferior vena cava-portal route, the superior vena cava-portal route, and finally the inferior vena cava long circuits from the spermatics or renals and through the portal-hepatic routes (Pleasants). Thus from the literature, the symptoms and signs varied from marked edema and ascites to none; from extensive evidences of collateral venous circulation to none; and even absence of albuminuria, despite thrombosis

of the cava with blockade of both renal veins. Simpson's analysis showed that in 50 per cent of the cases, all signs of caval obstruction were absent and thus, the diagnosis was made post mortem. He also believes that edema of the lower extremities, when present, is due to extension of the thrombosis into the iliac veins; or to renal or cardiac insufficiency. Evidences of collateral veins were present in twelve of the thirty renal cases and of these, seven showed extension of the thrombus into the right atrium. (Figure 1); in fifteen cases, ten showed albuminuria of which six showed only a trace. Involvement of the hepatic veins may result in jaundice and ascites. The former symptom was present in the case reported by Woodruff and Levine (16). The duration of the symptoms varied from three weeks to two years. This variability is similar to that found in renal tumors with and without renal vein involvement.

At the suggestion of Beer (17), the excretory urograms in cases of renal neoplasms were analyzed. In twenty-four cases in which the specimen and operative findings showed no involvement of the main renal veins, two cases, or 8.3 per cent, failed to visualize on the side of the tumor. In one of these cases, the pelvis was filled with blood clots and tumor. In nineteen cases with renal vein involvement, 78.9 per cent failed to visualize on the affected side. One of these patients showed no visualization of either kidney despite a blood urea nitrogen of 8 mgm. and fair excretion of indigo carmine from both sides cystoscopically. This patient at post mortem showed tumor thrombosis of both renal veins. This evidence is mentioned as a possible clue to the preoperative diagnosis of renal vein thrombosis.

OPERATIVE TREATMENT

From what has already preceded, one notes that certain cases with caval involvement may be suitable for surgical attack. Extensive thrombosis reaching into the heart and down to the iliacs is obviously inoperable. Smaller thrombi may be removed by the various methods to be described below.

Right-sided tumors may be approached through the ordinary Albarran incision. This exposure usually permits visualization of a good portion of the cava. Left renal tumors would best be removed through a transperitoneal incision, if one suspected preoperatively either renal vein or vena cava involvement. Thus far, the excretory urogram appears to be of value in suggesting renal vein thrombosis. After exposing the perinephric space, the presence of dilated veins should make one look for renal vein involvement. Our studies show a higher incidence of this engorgement, when the renal vein is invaded. The kidney is then mobilized and the pedicle isolated. The renal vein is freed and palpated for the presence of a thrombus. Should this be present, the renal artery and ureter are then tied and severed. The kidney and tumor are thus left

hanging by the thrombosed vein which is followed and separated. The cava is exposed and carefully palpated. From this point, the following procedures may be employed.

(1) A bud-like protrusion into the cava may be milked back into the renal vein which is then tied and severed central to the thrombus.

(2) The renal vein is opened close to the cava and the thrombus in the cava may be expressed through the opening or extracted with a curette or forceps.

(3) The cava is temporarily occluded by serrafine clamps above and below the thrombus.

The vessel is then incised longitudinally and the thrombus is extracted.

(4) In certain cases where a small localized invasion of the wall of the cava is present, the procedure of Rehn (18) may be employed. This consists of excising a portion of the wall of the vessel.

Closure of the opening in the cava is best accomplished by the use of interrupted or interlocking fine silk or catgut sutures. Should this procedure be unusually difficult, or the condition of the patient require rapid cessation of the operation, one can safely apply smooth, curved clamps to the opening in the cava. These clamps are left in place for five to seven days and after unlocking them for twenty-four hours, are easily removed. The use of packing to control the bleeding from the cava is unsatisfactory. Likewise, complete ligation of the cava above the level of the renal veins should not be done because of the almost certain fatal outcome.

ILLUSTRATIVE CASES

Case 1. History (Adm. 152780). A male 42 years old was admitted to The Mount Sinai Hospital on March 4, 1915 with a four months' history of constipation, frequency of and painful micturition. Four days before admission he noticed blood in his urine.

Examination. A mass was noted in the right hypochondrium. There was no edema of the lower extremities. Cystoscopy showed a normal left kidney, with good flow and strong excretion of indigo carmine from the left kidney. There was bleeding from the right kidney and the catheter was obstructed on this side at 22 cm. No flow of urine and no excretion of indigo carmine appeared through the right catheter.

Operation (Dr. Beer). Through a right lumbar incision an adherent kidney was exposed. It was three times normal in size. After mobilization, the ureter and renal artery were tied and severed so that the kidney remained attached by the renal vein. The latter was solid and about 1½ cm. in diameter. It was opened and was found to contain masses of tumor tissue which extended to the vena cava and across the midline towards the left renal vein. An attempt was made to dislodge the thrombus by milking it and using a curette. This was unsuccessful. The renal vein was therefore transfixed close to the cava.

Examination of the surgical specimen showed the presence of hypernephroma in the kidney and the renal vein. The patient responded poorly after operation and died. Permission for a post mortem examination was not obtained.

Case 2. History (Adm. 203010). A male, 61 years of age, was admitted to the hospital on July 30, 1920 with a six weeks' history of epigastric pain, anorexia and

loss of weight. During the preceding three years there were three attacks of hematuria.

Examination. The patient was a chronically ill man with a large, non-tender right kidney and dilated veins in both axillae. His hemoglobin was 68 per cent. The blood pressure was 110 systolic and 74 diastolic. The phenolsulphonphthalein test showed an excretion of 54 per cent in two hours. The blood urea was normal. On cystoscopy there was good excretion of indigo carmine from the left kidney but the right ureter was obstructed at twenty-five cm. with no flow and no indigo carmine. The right pyelogram suggested a tumor.

Operation (Dr. Hyman). It was performed through a right lumbar incision. There were large tortuous veins in the perinephric fat. The kidney was large, irregular and densely adherent. The renal vein and vena cava were solid for a distance of eight inches. The kidney was then removed after ligating the renal vein close to the cava. The latter was not opened.

The patient made an uneventful recovery and left the hospital nineteen days later. The specimen was reported "Papillary carcinoma." He was well four years and three months later.

Case 3. History (Adm. 237058). A male of 68, was admitted on December 10, 1923 with a seven months' history of intermittent hematuria and urinary retention due to clots.

Examination. The patient was an obese male in apparently good health with a large, firm, nodular mass in the right upper quadrant. There were no dilated superficial veins nor edema of the extremities. His blood urea was 15 mgm. per cent. The phenolsulphonphthalein test showed an excretion of 85 per cent in four hours. The blood pressure was normal. Cystoscopy revealed the presence of slight prostatic enlargement; a normal left kidney but a non-functioning right kidney.

Operation (Dr. Beer). It was performed through a transperitoneal incision disclosing a large, adherent right kidney about the size of a grapefruit. The renal pelvis was filled with tumor, and the renal vein was solid and extended across the spine. The kidney was then removed. The postoperative course was uneventful and he left the hospital after one month. The specimen showed the presence of a hypernephroma with involvement of the kidney pelvis and renal vein.

One month later, he was re-admitted with chills, fever and pains in the legs. The liver was enlarged and there was dullness over the right lower lobe. His temperature rose to 106°F. and a blood culture was positive for streptococcus hemolyticus. His condition grew worse and he died one week afterwards.

Necropsy Findings. At the point where the right renal vein entered the cava, there was an oval neoplastic nodule 2 cm. in diameter. This nodule involved the right lateral wall of the cava and partially occluded the vessel. Microscopically, this nodule was hypernephromatous. In addition, there were metastases to the branches of the right pulmonary artery.

Case 4. History (Adm. 238682). A male of 40 years, was admitted January 27, 1924 with a six months' history of recurrent total hematuria, dull pain in the right lumbar region and a loss of twenty-six pounds.

Examination. There was a mass in the right hypochondrium. At cystoscopy, the left kidney urine was clear but the right was bloody and the right pyelogram showed a deformity of the pelvis and calyces which suggested the presence of a neoplasm.

Operation (Dr. Beer). It was performed through a lumbar incision and a typical hypernephroma of the upper pole was found. This had broken through the capsule and become adherent to the adrenal. The renal vein, which was involved, was opened up near the vena cava and a tumor thrombus was milked back from the vena cava into the renal vein. The kidney was then removed. The specimen showed a

typical hypernephroma. The postoperative course was uneventful and he was discharged from the hospital nineteen days after operation. One year later he developed a local recurrence and he died three years following operation.

Case 5. History (Adm. 314320). A 63 year old male was admitted March 11, 1930 with a one year history of dysuria, hematuria, urgency and nocturia.

Examination. The patient appeared to be chronically ill. There was a large, ballottable mass in the left lumbar region, and a left varicocele which persisted in the recumbent position. Edema of the lower extremities was absent. Laboratory examinations were as follows. Blood Wassermann test was negative; the hemoglobin was 40 per cent; the blood pressure was 148 systolic and 68 diastolic, phenolsulphonphthalein excretion 20 per cent in six hours; and blood urea nitrogen 21 mgm. Cystoscopy revealed a normal right kidney with clear urine and good excretion of indigo carmine. There was no flow of urine and no excretion of the dye from the left kidney. The left retrograde pyelogram suggested the presence of a renal neoplasm. Excretory urography (performed two months before operation) showed a normal right kidney but practically no visualization of the left urinary tract. The patient refused operation. He returned, however, to the hospital two months later, when an X-ray examination of the chest, skull and long bones failed to show any evidence of metastases. At this time he agreed to an operation.

Operation (Dr. Beer). Through a left lumbar incision numerous engorged veins were disclosed in the perinephric fat. The kidney was found enlarged, adherent and full of tumor tissue. It was ruptured during its delivery. The renal vein was about 2.5 cm. in diameter and was filled by a thrombus. It was followed up to the vena cava which felt normal on palpation. After extirpating the kidney, a mass was felt along the spine. This was interpreted as involved lymph nodes. The specimen was 25 cm. long, 12 cm. thick and was filled with broken down tumor. Microscopy showed a carcinoma with clear cells, also invading the renal vein. On the third day following the operation, the patient developed circulatory collapse and died. The post mortem examination showed that the periaortic glands at the level of the renal veins were enlarged and fused in a mass which surrounded the aorta and vena cava. The right adrenal was enlarged to the size of a small orange and was completely replaced by tumor tissue which extended through the suprarenal vein and into the inferior vena cava where a carcinomatous thrombus, the size of a walnut, was adherent to the right lateral wall. The liver and lungs showed no evidence of metastases.

Case 6. History (Adm. 327660). A female 73 years of age, was admitted July 1, 1931 with a history of gastric disturbances, nausea and vomiting, of several years' duration. Two weeks before admission she developed swelling of the right leg. There was also a history of pain across the back and urinary frequency. Her physician found a mass in the right kidney region and referred her to the hospital.

Examination. A ballotable, slightly tender, globular mass was found in the right lumbar area. The right leg was swollen. The urine showed a three plus albumin and a few red and white cells and casts. The blood urea nitrogen was 38 mgm. per cent. Cystoscopy showed good excretion of indigo carmine from the left kidney. The right ureter was obstructed at 20 cm. and the dye excretion was faint from this side. Right pyelogram showed a deformity and filling defect in the pelvis. X-ray examination of the chest failed to show any metastases.

Operation (Dr. Beer). It was performed through a right lumbar incision. The kidney, which was the size of a grapefruit, was easily mobilized. The ureter and renal artery were then ligated and sectioned. The neoplasm extended into the pelvis and through the renal vein into the vena cava. The renal vein was opened near its junction with the cava and the thrombus was milked out from the cava into the opened renal vein. Following this procedure, the renal vein tore off. The cava was then closed with five plain catgut sutures and the wound closed in the usual fashion. The specimen was a typical hypernephroma.

Postoperatively, her condition became poor and she was given intravenous glucose by the drip method and a blood transfusion. The following day, her blood pressure was normal but her temperature rose to 105.2°F. and her urinary output dropped to two ounces in eight hours. The fourth day she had evidences of a bronchopneumonia. On the eighth day a few deep sutures were removed. This was followed by a discharge of some serum and gas bubbles. This serum on culture yielded B. Welchii, B. Coli and staphylococcus albus. Her condition grew worse, and she died on the tenth postoperative day.

Case 7. History (Adm. 226704). A female, 42 years of age, was admitted January 22, 1923 with a four weeks' history of loss of appetite and vomiting. For two weeks she had had pain in the right side of her chest, back and abdomen. Recently she noted hematuria and a loss of fifteen pounds in weight.

Examination. There was a large, hard, irregular and tender mass in the right upper quadrant. There were some dilated venules over the outer aspects of both thighs but no edema of the extremities. Over the base of the right lung there was some dullness and diminished breathing. Her blood urea nitrogen was 12 mgm. per cent; Wassermann test was negative; hemoglobin 90 per cent; blood pressure 120 systolic and 90 diastolic, and the phenolsulphonphthalein excretion was 35 per cent in two hours. Cystoscopy showed a normal left kidney with excretion of clear urine and strong indigo carmine. The urine from the right kidney was bloody and with no indigo carmine. A right pyelogram was attempted but the pelvis could not be filled.

Operation (Dr. Hyman). It was performed through a right lumbar incision. The kidney was enormously enlarged, adherent and covered with dilated veins. The pedicle was short, thick and infiltrated. The vessels were so glued together that they could not be isolated separately. The renal vein was infiltrated by tumor. The pedicle was clamped and the kidney was removed. This was followed by profuse bleeding from the depths of the wound which apparently came from some small veins which were found infiltrated by tumor. The vena cava felt solid, as though occluded by a thrombus. The patient's condition was so poor at this point, that one did not feel warranted in opening the cava. In addition, through an opening in the peritoneum, typical metastatic nodules were found in the liver. The patient failed to respond after operation and died in a few hours. The removed kidney was the size of a large grapefruit. The renal pelvis and vein were filled with tumor. The diagnosis was papillary carcinoma.

Case 8. History (Adm. 365576). A female, 42 years of age, was admitted to the hospital for the first time on November 10, 1932 for attacks of left loin to left groin pain which were associated with hematuria.

Examination. The patient was obese, weighing 228 pounds. There was some left costovertebral tenderness. The urine was grossly bloody. Her blood urea nitrogen was 7 mgm. per cent. A flat plate of the abdomen was negative for calculus in the urinary tract. Cystoscopy showed a normal bladder. The left kidney excreted strong indigo carmine. The right kidney urine showed a slightly weaker concentration of dye and the urea concentration on this side was half that on the left. A wax bougie was passed up the left kidney and was found to be positive. She was discharged from the hospital to the follow-up clinic.

In August 1933 she was re-admitted with the same symptoms, but, in addition, she complained of rectal pain and bleeding. Cystoscopy and a left pyelogram were done and found to be normal. The right kidney excreted concentrated indigo carmine. Her urine was negative for uric acid crystals. Because of the negative urological findings, a hemorrhoidectomy was done for the internal hemorrhoids.

The symptoms on the left side persisted and an excretory urogram was done on March 21, 1934. The excretion from the left side was insufficient for diagnosis. The right kidney was considerably enlarged and the pelvis and calyces appeared to be

somewhat deformed. A right retrograde pyelogram was therefore done, and a markedly distorted pelvis and calyces were found which suggested the presence of a neoplasm. She was re-admitted to the hospital. At this time there was no edema of the extremities, the right kidney was palpable and she had lost twenty pounds in weight.

Operation (Dr. Beer). It was performed, under spinal anesthesia, through a right lumbar incision. The lower half of the kidney was enlarged and adherent. The renal vein was filled with tumor and formed an ovoid mass the size of an apricot. All the attachments were severed so that the kidney was left hanging by the renal vein. The vena cava was exposed and found to contain a mass which extended upwards for two and one-half inches towards the diaphragm. Within it the upper end of a rounded mass was palpated. Below the entrance of the right renal vein, the thrombus extended for about half an inch. The renal vein was cut close to the cava and an unsuccessful attempt was made to express the thrombus through the opening. Then by morcellation and repeated milking of the cava from above downwards, a large mass of organized tumor tissue was removed from the cava. A finger was then introduced into the cava but no further thrombus was felt. The lateral opening in the cava was therefore closed with a fine interlocking plain catgut stitch and the bleeding was controlled. The usual wound closure and drainage was used. The postoperative course was uneventful and she was discharged to the follow-up and radiotherapy clinics. The specimen removed was a malignant Grawitz tumor of the hypernephroid type. The subsequent history of the case was as follows:

In July 1934—A small local recurrence was felt. In November 1935 a few small nodules were felt in the scar. Roentgenograms of the chest and long bones were negative. By this time several courses of X-ray therapy had been given. In March 1936 she developed brawny edema of both lower extremities and dilated superficial abdominal veins. In December 1936 she was admitted to another hospital with a cough, expectoration of blood-streaked sputum, pain in the back and a loss of twenty pounds in weight. She had ascites, a large liver, edema of the lower extremities and an icteric tint to the sclerae. Roentgenograms of the chest and pelvic bones showed no abnormalities. Her urine had a specific gravity of 1010 with a faint trace of albumin and a few pus cells. The serum bilirubin was 1.3 mgm. per cent. She died on January 1, 1937. The post mortem examination revealed an occlusion of the inferior vena cava by tumor. Metastases to the liver and suprarenals were also present. There were no gross pulmonary metastases but microscopically there was tumor tissue in a number of veins but not in the parenchyma.

Case 9. History (Adm. 405580). A female, 69 years of age was admitted March 9, 1937 complaining that during the previous year she noted weakness, frequency of urination and a loss of forty pounds in weight. Three months before admission, she was investigated at the consultation clinic at the hospital and was found to have a large stone in the right lumbar ureter. At that time she was cystoscoped and was found to have an obstruction in the right ureter at 20 cm. with no flow of urine and no excretion of indigo carmine.

Examination. There was an emphysematous chest and a moderate enlargement of her heart, but no other findings.

Laboratory Data: Blood pressure was systolic 130 and diastolic 80; hemoglobin 60 per cent; phenolsulphonphthalein excretion, 60 per cent in four hours; blood Wassermann, negative; urine, cloudy with many pus cells; blood urea nitrogen 8.0 mgm. per cent; excretory urography showed a normal left urinary tract but no function on the right side.

Operation (Dr. Hyman). It was performed through a right lumbar incision. A large network of dilated veins was present in the perinephric fat. The lumbar ureter was easily exposed without mobilizing the kidney and the stone extracted.

However, in view of the fact that no indigo carmine appeared through the ureter-
otomy wound in twenty minutes after its administration and also, because of the
dilated veins in the perinephric fat, it was decided to expose and mobilize the kidney.
The twelfth rib was resected and a neoplasm occupying the upper two-thirds of the
kidney was found.   Part of the adrenal remained adherent to the tumor after mobiliz-
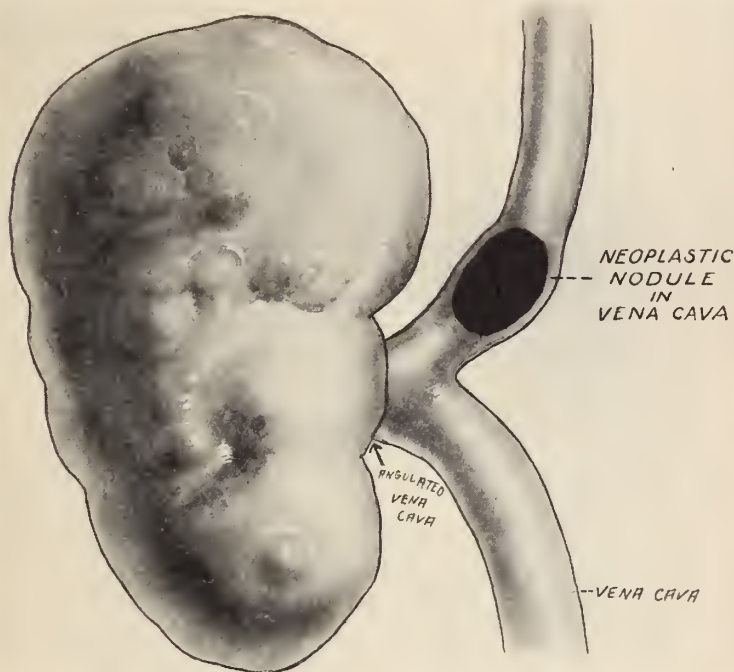
FIG. 2 (Case 9)

FIG. 3 (Case 9).   Appearance of vena cava after nephrectomy and removal of
tumor nodule.

ing the kidney.   Careful exposure of the renal pedicle revealed the fact that the vena
cava was so angulated by adherence to the kidney as to form a "V" with the apex at
the hilum of the kidney.   This vessel was at first considered to be the renal vein.
The latter was only half an inch in length.   After the pedicle was transfixed, cut
through and the kidney ablated, the vena cava straightened out.   Palpation of the

vena cava now showed the existence of a nodule the size of a large olive within the lumen. Two temporary ligatures and serrefine clamps were placed on the cava above and below the nodule. The cava was then deliberately opened and the tumor nodule was removed with a blunt curette from its attachment to the intima. The opening was then sutured with vaselinized silk in interrupted sutures. The wound was closed with rubber dam drainage. During the procedure the cava had been compressed for twenty-two minutes. The patient's condition remained satisfactory throughout the operation (Figs. 2 and 3). The subsequent course was very satisfactory and she was discharged on the nineteenth postoperative day. When last examined, eight months after operation, the patient was found to be in excellent condition. Examination of the specimen showed that the upper two-thirds of the kidney was replaced by a yellow nodular tumor which infiltrated the capsule. A cut section showed irregular areas of hemorrhage and necrosis. A mass the size of a peach was easily separable from the main tumor at the upper pole. Microscopically the tumor in the kidney was a malignant Grawitz tumor-clear cell carcinoma type. The mass above the kidney possibly represented a metastases to the adrenal. The mass from the vena cava was mainly necrotic tumor and organizing thrombus with iron and calcium deposits.

Case 10. History (Adm. 283818). A female, 37 years of age, was admitted September 25, 1927 complaining of swelling of her legs and abdomen and shortness of breath. Her illness began eight months previously with swelling of her ankles which gradually progressed upwards. Recently, dyspnea, oliguria, polydipsia and amenorrhea were noted.

Examination. The patient was emaciated and jaundiced. Her abdomen was markedly distended with fluid; the superficial abdominal veins were dilated, forming a "caput medusa" around the umbilicus. The liver was enlarged and a ballotable mass was felt in the right upper quadrant. There was marked edema of both the lower extremities which extended upwards to involve the sacrum, lateral abdominal walls and the back, as high as the lower chest.

Laboratory Data: Blood pressure was systolic 140 and diastolic 118, urine, acid, specific gravity 1022, a faint trace of albumin, bile and urobilin was present, few red and white cells and hyaline casts; blood Wassermann, negative; icteric index, 28; Van den Bergh; direct positive, indirect 1 to 50,000 with 2.0 mgm. of bilirubin; blood urea nitrogen 22 mgm. per cent; Bromsulphalein test showed a retention of 50 per cent in half an hour; phenolsulphonphthalein test showed 60 per cent excretion in five hours. Paracentesis abdominis was performed and $6\frac{1}{2}$ liters of slightly greenish fluid were removed. A pneumo-peritoneum showed a moderate enlargement of the liver and a normal sized spleen. Her condition became progressively worse with a gradually mounting pulse rate and she died ten days after admission. Post mortem examination showed a hypernephroma of the left kidney extending into the inferior vena cava through the renal vein. The thrombus in the cava extended from the femoral veins below to the right auricle above. There were metastases in the lungs (Fig. 4).

Case 11. History (Adm. 297359). A male, 45 years of age, was admitted for the first time on December 3, 1928 complaining of swelling of his legs and abdomen. This developed seven weeks before admission. A few weeks prior to this, he noted pain in the left chest, left lower abdomen and urinary frequency.

Examination. There was dullness over the right lower lobe of the lungs; a large abdomen with a fluid wave and shifting dullness; dilated abdominal wall veins which extended down over the lower extremities and up over the chest wall; and swelling of both lower extremities.

Laboratory Data: Hemoglobin was 62 per cent; blood pressure 124 systolic and 90 diastolic. Six consecutive urines after admission showed an occasional pus cell

with a faint trace of albumin and a specific gravity up to 1024; blood urea nitrogen 15.0 mgm. per cent; blood Wassermann, negative; and Van den Bergh reaction, normal.

Cystoscopy was carried out and both ureters were catheterized without encountering any obstruction. Indigo carmine appeared from both sides in good concentration. A right pyelogram showed deformity of the pelvis and calyces which was thought to be due to under-injection of the pelvis. The pyelogram was repeated one week later and the same deformity was present. Exploratory operation was advised but the patient left the hospital against advice. He was re-admitted twelve days

Fig. 4 (Case 10). Hypernephroma of the left kidney extending into the inferior vena cava through the renal vein. Thrombus extended from the femorals below to the right auricle above.

later. The abdomen was larger and there were more marked evidences of the development of collateral circulation in the abdominal wall. The abdomen was tapped and four liters of clear ascitic fluid were removed.

Operation (Dr. Beer). Exploratory laparotomy was then performed. The liver was enlarged and violaceous. At the upper pole of the right kidney a neoplasm was found which seemed to involve the inferior vena cava and aorta. The case was considered inoperable and the abdomen was closed. He developed signs of circulatory failure and died three days after operation. At the post mortem examination the left kidney was found to be normal, as well as the renal vein. The right kidney

was twice the size of the left and was adherent to the vena cava and liver. The upper third of the kidney was replaced by a soft yellowish, necrotic tumor which had broken into the renal pelvis and renal vein. It then extended through the latter into the inferior vena cava which was twice normal in size and was filled with necrotic tumor from the iliac veins to the right auricle. All the heart chambers were normal except the right auricle which was filled with necrotic yellowish material. The liver was enlarged and congested. The larger hepatic veins were filled with tumor thrombi. The final diagnosis was tubular carcinoma of the right kidney with infiltration of the inferior vena cava, right auricle and hepatic veins; metastasis to right lower lobe of lung (size of a pea); and emboli of the pulmonary arteries (some contained tumor cells).

SUMMARY AND CONCLUSIONS

1. From the material herein described it is quite obvious that there is a definite incidence of involvement of the inferior vena cava in renal neoplasm in adults. The commonest mode of involvement is by extension from a thrombosed renal vein. There may also occur a direct invasion of the wall by contiguity with the tumor or rupture of a metastasis into the cava.

These cases may remain unrecognized clinically, as signs of caval obstruction may be absent even in instances of complete occlusion of this vessel.

2. At least one-third of the known cases developed through extension of a left renal neoplasm through the renal vein. The thrombi in the vena cava become infiltrated with neoplastic cells. However, large tumor thrombi may exist in the vessel without infiltration of the wall. On the other hand, emboli and metastases may be absent even in extensive tumor thrombosis of the vena cava.

3. Deliberate surgical removal of such thrombi has been practiced successfully. Several instances of five year cures in this type of patient have been reported in the literature. In our cases two lived approximately three years and one lived over four years.

4. Laboratory tests of renal function may be normal even with complete occlusion of the inferior vena cava above the renal vein.

5. Non-visualization by excretory urography in renal neoplasms with vein involvement is of diagnostic significance.

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LOCAL BLOODLETTING IN OPHTHALMIC PRACTICE

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Local bloodletting is a time-honoured remedy, which has fallen into disuse in recent years, being replaced by other methods, more in keeping with newer concepts. However, it is a potent remedy, followed by instantaneous relief of pain, and also influencing the course of the inflammation. It was practiced by the application of leeches, which mode was abandoned as not compatible with the ideas of antisepsis (although I have never heard of or seen any ill effects from the application of leeches), so that nowadays one can not find leeches in a modern drugstore. This led to the development of the "artificial leech", a trephine-like knife which, quickly rotating, cuts through the cutis, and produces one or several sharp-edged, circular, profusely bleeding wounds. The place of application of leeches and the artificial leech was usually the temple; natural leeches were sometimes applied under the eye.

That local bloodletting is no longer in the armamentarium of the modern ophthalmologist was apparent to me, when a few years ago I heard a paper read in which mention was made of the beneficial effects of leeches used under the eye in cases of scleritis or episcleritis. At that time I mentioned that I often used local bloodletting at the site of the trouble.

Bloodletting is beneficial in a number of eyetroubles in which congestion is a prominent symptom, and in some in which it is not.

The following are the conditions in which it is particularly efficient, and I will describe the mode of my procedure. While I am not the only one practicing bloodletting at the site of the trouble, I do not think that it is in general use, or that even many of my colleagues are cognizant of the method.

Persistent episcleritis is a torpid localized congestion and swelling of the episclera and sclera, lasting from six weeks to several months. It is benign, sometimes painful, and has been variously ascribed to rheumatism, gout and tuberculosis. I advise letting it come to full development and especially not to mention bloodletting to the patient at his first visit. After the patient realizes its chronic nature, he will be more willing to submit to the procedure.

It is performed with a sharp pointed iris scissors. The patient is directed to turn his eye in, if the episcleritis is temporal, out, if it is nasal. The eyeball may be held with bare index finger and thumb between the

separated lids. Cocain should not be used on account of its vasocon-
stricting effect, which would prevent profuse bleeding and therefore defeat
the object of the operation. The desirability of profuse bleeding is also
the reason why the scissors should be very sharp. The scissors should be
opened 6–7 mm. wide, directed at a tangent towards the sclera, and with
a quick cut a V-shaped wound is produced through conjunctiva and
episclera. No bandage is necessary. This will in most cases dispose of
the episcleritis. Occasionally I find it necessary to repeat the performance
after a week's interval. There is no possibility of cutting through the
sclera. Anybody who prefers a knife may take a razor-sharp scalpel
and with quick cuts (holding the knife lightly between his fingers) make
a cross cut through the nodule. I do not believe there is a possibility of
cutting into or through the sclera.

Iritis and iridocyclitis (of any etiology), especially such with dark con-
gestion, will be favorably influenced by local bloodletting. With the
sharp iris-scissors several cuts, 7–8 mm. from the limbus are made on the
lower half of the eyeball. Also the effect of atropin on the pupil is greatly
enhanced by the bloodletting.

Chronic trachoma with exacerbations: The upper lid is everted, and a
very sharp scalpel is lightly drawn over the conjunctiva and tarsus; two
or three cuts are made straight across, especially in the more vascular
furrow 2 mm. from the lid edge. Then the patient is directed to look
down, and the lower lid is slipped under the upper to protect the eyeball.
The knife is turned with the edge upwards, and several cuts are made
blindly as near as possible to the fornix, and further down. The knife
must be lightly held, and must be very sharp. If it were not very sharp, it
would defeat the object of the proceeding (which is profuse bleeding) and
scar formation would result. If correctly performed, no scars result.
The lower lid is treated the same way.

Subacute conjunctivitis. The same proceeding is used as in trachoma.
Patients are frequently greatly relieved, and demand performance of the
scarification. It has always been a mystery to me, that a very congested
conjunctiva not only immediately becomes very pale after a little blood-
letting, but may remain so for at least several hours. The good effect
can be noticed even after two days.

Relapsing abrasion of the cornea. This troublesome affection of the
cornea, occurs especially in cases where a cinder has been removed by
scraping, but also after other types of trauma. Relapsing abrasion
is certainly known to every practicing ophthalmologist. The underlying
pathology is obscure, but it seems related to herpes. How obscure it is,
is evidence by the fact, that Schieck and Brueckner's Handbook devotes
many pages to it, after the perusal of which the reader is left with the
distinct conviction that one does not know anything certain about it. My
teacher, Arlt, whose therapy after 60 years is unexcelled in most instances

to this very day, recommended that the eye be bandaged for about five days, after which the abrasion usually remains healed until the next recurrence. By some obscure reasoning, considering that the seat of the trouble is the conjunctival layer of the cornea, I tried scarification of the conjunctiva, with brilliant result in most cases. After the scarification the lids are slightly brushed with $\frac{1}{4}$ per cent nitrate of silver solution, and the eye left unbandaged. The graver forms of this trouble, with blister formation, loosening of the epithelium of the whole cornea and hypotony, do not yield such striking results, but are favorably influenced by this treatment.

RETROPERITONEAL ABSCESS WITH OBSCURE CLINICAL MANIFESTATIONS

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The subject of retroperitoneal abscess is one in which Dr. Beer has been greatly interested. This is shown by the fact that, in 1930, Dr. A. Hyman reported from Dr. Beer's service at The Mount Sinai Hospital, a series of cases under the title: "Suppurative Retroperitoneal Pelvic Lymphadenitis." Of varying etiology (sometimes without known cause) the features of the lesion as noted by Hyman were fever, often of low grade, pain, gradual development of psoas spasm, and the appearance of a mass in the iliac region. Rectal or vaginal examination revealed tenderness and often induration or fulness on the affected side. He refers to cases in which a retroperitoneal abscess remained undiagnosed until rupture into one of a number of viscera occurred, or until disclosure by autopsy. Although he does not discuss clinical features, Hyman clearly recognizes cases of retroperitoneal abscess which can be readily diagnosed and treated, and others in which diagnosis and management may be difficult. The latter group is of particular interest to me because such cases have been under my care and have proven serious problems in diagnosis and treatment. Two cases of the variety which I have in mind, namely those with obscure clinical manifestations, were on my service this year. I have thought it worth while to report minutely these two current cases, while they are fresh in mind, together with an earlier one which is vividly remembered, because only from a detailed description can one realize the difficulties in diagnosis and treatment which are inherent in this important yet little known type of retroperitoneal infection.

As will be seen from a perusal of these cases, there are certain general features common to all three (and, indeed, to all the cases which I have seen). It is, however, the composite of the individual features which in each instance comprises the difficulties which arose at the bedside. In the case reports I have therefore adhered closely to the bedside notes made by myself and others, for they portray best the actual problems which were encountered.

ILLUSTRATIVE CASES

Case 1. History. (R. K., Adm. 278798). The patient was twelve years old when admitted on April 17, 1927. Her previous history was

irrelevant. Three weeks before admission she fell on her back while dancing. She arose, continued dancing and there was nothing in the subsequent course, except the time element, that would relate the fall to the clinical condition. Three days after the fall there began a complaint of pain about the right knee, and this remained the most striking feature in the subsequent clinical course. It was intermittent, ofttimes severe enough to require the administration of opiates by the attending pediatrician, Dr. Murray H. Bass. A few days after the onset of pain, low fever developed; it remained low grade throughout. Shortly thereafter, spasm at the right hip appeared, and became almost as prominent an aspect of the clinical picture as the recurrent pain in the region of the right knee. No other symptoms developed. Repeated X-ray examinations of the spine and pelvis were negative. The child was examined upon many occasions before admission to the hospital by Dr. Bass, other consultants and myself, and presented little, if any, variation from the following: the abdominal examination was negative, with possibly occasional fulness just above right Poupart's ligament. There was tenderness in this region, but at no time a palpable mass. There was possibly occasional fulness in the pelvis on the right side, as noted by rectal examination. Spasm was present at the right hip, the thigh held flexed. There was hyperalgesia along the back of the thigh and leg in the general distribution of the sciatic nerve. Blood counts were not informative.

Operation was decided upon in the nature of an exploration of the retroperitoneal space rather than on the basis of a diagnosis, although the belief that there was a suppurative focus somewhere along the anterior surface of the ilio-psoas appeared warranted, even in the absence of any confirmatory evidence. It did not seem justifiable to wait any longer before proceeding with operation because there had been no evidence pointing towards the possibility of a definitive diagnosis during the three weeks' period of careful observation before admission to the hospital.

At operation on hospital admission, April 17, 1927, a long incision parallel to and somewhat above the crest of the ilium was made, and was deepened through external oblique and musculature to the peritoneum. The peritoneum was stripped towards the mid line, exposing the psoas. The anterior surface of the muscle was then bared by additional stripping of peritoneum. No abnormality was noted. In view of the completely negative findings, the exploratory operation was about to be discontinued when a small whitish area over the inner border of the psoas muscle was noted. This was bluntly entered and pus was encountered. Upon enlarging the opening, an abscess of substantial proportions was found to lie in the gutter running longitudinally between the mesial border of the psoas and the lateral aspect of the bodies of the lumbar vertebrae. The abscess extended into the pelvis over the iliacus muscle. When the right leg was extended old blood clots mixed with pus welled up from the most

dependent part of the abscess cavity. The suppurative tract was laid wide open throughout its length. The cause of the abscess was sought for but not found. The musculature appeared normal, the bodies of several vertebrae, although laid bare, presented no abnormality, and the intervertebral discs appeared normal. Inspection of the anterior wall of the cavity for a possible etiologic factor, was also negative. Drainage was by gauze and rubber dam. It was obvious that drainage into the bottom of the pelvis was not ideal, but a counter incision through the vagina was unwarranted. The bacteriological report on the pus was streptococcus, which failed to grow after several attempts at transplantation.

In view of the history of trauma and the existence of blood clots in the bottom of the abscess cavity, the diagnosis of a retroperitoneal abscess derived from an infected hematoma appeared probable.

There was rapid subsidence of pain at the knee, and somewhat slower recession of the spasm at the hip. Temperature was soon normal. Drainage was maintained to the bottom of the wound for several weeks in order to avoid retention. Progressive healing from the bottom appeared to take place. The patient was discharged with a clean, superficial, granulating wound.

The further history of the case deals with a recurrence of suppuration in the general region of the old operative field, either referable to pseudo-healing rather than actual healing in the original field, or to recurrence following trauma. The child was entirely well throughout 1927 and 1928 until mid-December. She then slipped on a staircase, bruising her right knee. Two days later there was onset of pain in the right lower thigh, soon followed by psoas spasm. From that time to the time of readmission and operation two and a half weeks after the accident, the symptoms and signs were an exact replica of the original story.

Second Operation. Only under anesthesia was a mass felt. It appeared to be situated in the anterior portion of the old scar. After some difficulty, because of cicatricial tissue, the peritoneum was exposed and stripped away from the psoas. Scar tissue over the muscle was incised and a collection of pus, sharply limited by a dense membrane, was entered. The abscess seemed to be partly on and partly in the mesial portion of the psoas muscle, extending to the iliac vessels. The abscess cavity and wound were widely packed. After operation pain and psoas spasm cleared up, fever soon subsided, packings which had been inserted into the abscess cavity were progressively shortened, and the patient was discharged with a clean, granulating wound. Healing, however, did not occur. On one occasion unhealthy granulations, which occupied much of the wound, were curetted away. Prolonged immobilization, the application of various ointments, were of no avail. It was finally decided to reexplore the wound in order to determine the reason for non-healing, and this was done on June 20, 1929, about six months after the pre-

vious operation. The old cicatrix was incised, some purulent material was encountered, and the incision was deepened to the extra-peritoneal space. The region of the psoas muscle was then exposed. Its surface was found to be covered by unhealthy granulation tissue. On its mesial aspect a pocket of granulation tissue was encountered and was curetted away. There were several similar pockets in that region. With care taken to avoid injury to the iliac vessels, the mesial and under surface of the psoas muscle was explored. Here a large pocket of pus and infected granulation tissue extending beneath both psoas and iliacus was encountered. There appeared to be no way of draining adequately this pocket other than by transection of the psoas. Accordingly, the psoas was divided transversely. The abscess, situated between the psoas and that portion of the ilium lateral to the sacro-iliac joint was freely opened thereby. Bare bone was not encountered. The cavity was widely packed. It was my impression that the abscess beneath the psoasiliacus represented either the ancient undrained or a part of the inadequately drained abscess.

The course after this final operative procedure was entirely satisfactory. The wound was permitted to heal slowly from the bottom. It has remained healed since that time, and there has been no recurrence of any manifestations. Difficulty in walking, due to severance of the psoas, was gradually compensated for, and gait has been normal for a long time. Follow-up has been closed for several years, but mention can be made of the fact that the patient was seen very recently and has been found to have remained well.

Case 2. History (H. C., Adm. 406869). The patient, who was five years old, was admitted to The Mount Sinai Hospital on April 8, 1937. Her previous history was irrelevant. Five months before admission there was a complaint of occasional pain in the right hip. A slight limp was noted. These manifestations were intermittent, so fleeting that the parents paid little attention to them. The child was otherwise well until five weeks before admission, when there was complaint of chilly sensations and malaise. A temperature of 102°F. was noted. From time to time there was recurrence of fever and chilly sensations, the child being in bed for part of this period. Pallor was first noted about three weeks before admission and had been progressive. For three to four days before admission pain in the right hip became persistent and progressively more severe. The child was referred to the hospital because of fever of unknown origin, pallor, and pain in the right hip.

The admission diagnosis was rheumatic fever (probable). A few days after admission a non-tender firm mass was felt above the right inguinal fold, and fever reached a higher level. Pain in the right inguinal region became more marked. To some, the mass vaguely felt in the region of the right Poupart's ligament, was inflammatory, and to others, neoplastic.

One week after admission there was considerable difference of opinion as
to whether the mass was smaller or larger, tender or not tender. In other
words, there was no definite evidence of progression of the lesion, and
there was no evidence of its relationship to the febrile course. Spasm at
the hip was slight and had not progressed or retrogressed during the
hospital stay.

I saw the patient for the first time twelve days after admission, and
diagnosed an extraperitoneal inflammatory process above Poupart's
ligament which I believed might become more superficial. The diagnosis
was made neither on the basis of a mass (which could not be felt), nor on
the presence of a number of discrete, enlarged lymph nodes, but on the
basis of observation in other cases in which such slight evidence went with
an extensive retroperitoneal infection. I suggested poulticing for several
days in the hope of rendering the retroperitoneal lesion more superficial
for drainage. I saw the child again three days later, at which time the
swelling was perhaps somewhat more elastic; but there was no evidence of
any tendency towards superficial localization of an abscess. I expressed
the opinion that exploratory operation for probable retroperitoneal ab-
scess was indicated and proceeded with operation the same day. The
preoperative note was as follows: The obscure course with low fever and
minimal manifestations referable to the affected region, is characteristic
of a type of retroperitoneal abscess with but few external evidences of its
existence. The local findings in this case were: A suggestion of a mass
with a sense of resistance in the left lower quadrant directly above Pou-
part's ligament; tenderness in this region but no palpable mass as such;
no definite signs of an elastic swelling and no intrinsic evidence that the
lesion was a suppurative one; also, no etiological factor, careful inquiry
having been made as to the possibility of a preexisting infection.

Operation. It was noted that the mass was no more clearly defined
under anesthesia. A two inch incision was made just above and parallel
to Poupart's ligament, its mesial end being placed approximately over
the site of the iliac vessels. The external oblique was incised and the cut
margins retracted. It was interesting to note that no edema of the under-
lying musculature was to be discerned. The position of the iliac vessels
was determined by palpation in order to traverse safely the musculature
at a position just lateral to them. In the depths infiltrated tissue was
encountered, was traversed bluntly, and suddenly a large collection of pus
under tension was entered. Deep retractors were inserted in order to
ascertain the situation and the limits of the abscess cavity. The latter lay
directly outside the peritoneum. Its floor was the psoas muscle covered
by exudate, and the tract extended upwards about four inches from Pou-
part's ligament. The external iliac vessels, covered by exudate, com-
prised part of the mesial wall. Although there were a few small recesses,
the abscess was essentially unilocular. It should be noted that the ab-

scess did not extend mesially over the inner edge of the psoas muscle and did not extend downwards below Poupart's ligament.

Broken down lymph nodes were not observed. Indeed, no information concerning the etiology of the abscess could be obtained either from the appearance or from the situation. The infection could have been derived from the vagina, the lower extremities or the peritoneal cavity. Only on the law of probability could one guess that the abscess was secondary to some infection of the iliac lymph nodes from some source which they drain. With retractors in place, the abscess cavity was snugly packed with gauze. The report on the culture of the pus was hemolyticus streptococcus beta.

The postoperative course was uneventful. Fever rapidly subsided, hip spasm soon disappeared and the child was soon convalescent. When last seen at Follow-Up on October 5, 1937 the child was entirely well with a healed wound.

Case 3. History (A. Z., Adm. 407894). The patient, who was forty-two years old, was admitted on April 29, 1937 with a history that five days before admission an inflamed blister was noted between the fourth and fifth toes. It soon ruptured spontaneously, but beyond it a few red streaks were noted. The next day there was a severe chill with high fever, and several nodules were noted on the foot and leg. These were surrounded by areas of redness. On the third day before admission, there developed pain in the left lower abdomen immediately above Poupart's ligament. Fever persisted, there was another severe shaking chill, and shortly before admission there developed increasing difficulty in urination as well as some dysuria.

The admission note describes an acutely ill patient of septic appearance with apparent dyspnea and some slight cyanosis. On the left foot and leg there were a number of tender, red, superficial nodules interpreted as areas of lymphangitis or cellulitis. Although there was no tenderness over any of the venous trunks of the extremity, there were inflamed lymph nodes in the inguinal and saphenous areas. Over the skin immediately above Poupart's ligament, there were two superficial red streaks. Beneath them there appeared to be exquisite, superficially situated tenderness without abdominal rigidity. The impression which was gained was that the patient was suffering from a dermatophytosis from which a lymphangitis and an inguinal and retroperitoneal lymphadenitis were derived.

Fever began to subside shortly after admission, chills did not recur, improvement set in, and the immediate problem appeared to be one of management of urinary retention. The patient was transferred to the Dermatological Service for the treatment of the dermatophytosis. For the following week urinary retention was the outstanding manifestation and this was studied by Dr. Beer's service because the question of a diverticulum of the bladder had been raised. The studies made by his service led to the opinion that an extravesical lesion existed.

About twelve days after admission, at a time when the patient suffered but little fever, there was noted for the first time a mass, directly above Poupart's ligament, which was tender, and consisted essentially of enlarged, discrete, lymph nodes. There was no evidence of suppuration, and in view of the improvement in the patient's condition, spontaneous subsidence appeared probable. In the succeeding days fever rose to a somewhat higher level, but the mass did not progress towards abscess formation. It had not increased in size, there remained a number of discrete lymph nodes which capped the mass, and local tenderness was minimal. Punctate areas of suppuration within individual lymph nodes were visualized as a possibility or probability, but an abscess could not be diagnosed. Indeed, it was my opinion that spontaneous resolution might occur even at this stage.

On May 18, twenty days after admission, the mass was noted to still consist essentially of a series of inflamed lymph nodes without any evidence of coalescence. Indeed, the mass was less tender and somewhat smaller. But fever was now beginning to assume a remittent character. On May 20 a diffuse infiltration on the left side of the pelvis, which had been felt by rectum on a few occasions, localized into a mass to the left of the rectum which was tender on pressure and of soft consistency. It was this mass which led to the impression that pelvic suppuration existed. Operation was decided upon on May 21, not because the external mass had changed in character, but because the rectal examination offered the lead as to the likelihood of a pelvic abscess and because fever rose to a higher level (105.2°F.) on this day. It should be added that spasm at the left hip appeared for the first time on May 20, and that blood counts made upon a number of occasions suggested the existence of suppuration.

The preoperative note indicates best the difficulties of diagnosis and therapy. It was as follows: The interpretation of the nature of the inflammatory process, which obviously existed in the left lower quadrant, was quite difficult because the lesion appeared to wax and wane, and because at no time did anything in the nature of a frank suppurative area appear. Indeed, spontaneous subsidence seemed likely for a considerable period of time. Although there was some doubt in the minds of a number of those who saw the patient as to the nature and origin of the lesion in the left lower quadrant, it seemed to me that the diagnosis of an infection of the iliac lymph nodes derived from the infection of the foot, appeared warranted. Only in the last day or two did hip spasm appear, and this alone justified an exploration for a suspected retroperitoneal abscess. The mass itself, if so ill defined a sense of resistance can be termed a mass, did not change appreciably (this refers to a sense of resistance above Poupart's ligament and not to the conglomeration of inguinal lymph nodes). It was still no more than a sense of resistance which rose from the region of the inguinal canal to terminate indistinctly about two inches above Poupart's ligament.

Operation. An incision was made parallel to and a short distance above the inguinal canal. The external oblique aponeurosis was divided in the line of the skin incision and its margins retracted. The sense of resistance above Poupart's ligament was no more clearly defined beneath the external oblique than beneath the unopened skin. In other words, if in fact an abscess existed, it had no parietal representation, so to speak, but was situated essentially toward the posterior part of the pelvis. The external oblique musculature appeared edematous. It was cautiously entered with a closed scissors, and was traversed. When the scissors were opened, pus began to well up. A dressing forceps was now introduced. There then escaped under tension about four ounces of pus. Retractors were inserted and the abscess was found to lie between the psoas muscle and the posterior peritoneum. The latter was mobilized for the full exposure of the suppurative tract. The latter extended upwards a considerable distance. Indeed, its upper limits were not clearly defined, for it reached at least five inches above Poupart's ligament. In addition to this portion of the abscess lying on the psoas muscle, there extended mesially over the inner border of the psoas, and into the true pelvis, another purulent tract. This appeared to reach the region of the bladder and (or) rectum. Below, the abscess terminated abruptly at Poupart's ligament where the external iliac artery lay exposed. No connection with the femoral region could be discerned. The two suppurative tracts were emptied of pus and were widely packed. Culture of the pus revealed hemolyticus streptococcus beta.

In commenting on the operative findings, my note stated that the great extent of the abscess as well as its multiple ramifications could not have been suspected from the physical examination. I assumed that the abscess must have existed as such for a considerable period of time. There was no evidence at operation that it was derived from infected lymph nodes but, on the basis of the apparent etiology, iliac lymphadenitis was the probable source of the extraperitoneal abscess.

The postoperative course was uneventful. The patient became afebrile promptly, the deep wounds were permitted to heal from the bottom, and the patient was discharged symptom free. When seen at follow-up on September 7, the wound was healed, but a hernial defect at the site of operation existed.

RECESSION OF RENAL AMYLOIDOSIS DUE TO MULTIPLE SKIN GANGRENE ASSOCIATED WITH ARTERITIS OF THE SKIN

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Amyloidosis has been looked upon by clinicians as an irreparable, often terminal, complication of some severe chronic wasting illness, such as tuberculosis, chronic broncho-pulmonary disease, osteomyelitis, sepsis or malignancy. Virchow (1), who first clearly described this condition, indicated that he thought that, once laid down, amyloid remained unchanged. As early as 1880 Kretzschmer and Westbrook (2) and later Owen (3) cited clinical examples of apparent cure of amyloidosis. In 1891 Gardner (4), in a discussion of a paper on renal disease by Delafield, quoted the following instance: After the amputation of a leg that had been the seat of an extensive osteomyelitis, apparent recession of an amyloidosis and the disappearance of albuminuria supposedly due to an amyloid kidney occurred. The possibility of amyloid deposits disappearing had gained experimental support by the studies of Litten (5) as early as 1885. He showed that pieces of tissue containing amyloid lost this deposit when placed into the peritoneal cavity of experimental animals. These conditions were, of course, quite different from those which occur normally and the reaction was more in the nature of a response to a foreign body. In 1907 Dantchakow (6) showed conclusively that amyloidosis of the salivary glands of rabbits caused by chronic staphylococcus infection was resorbed when the infection was completely extirpated. In 1912 Herringham (7) cited a case of amyloidosis which recovered clinically after the cure of suppurative disease of the hip joint. Kuczynski (8), in 1922, reported the experimental production of amyloidosis by the repeated injection of nutrose and in 1923 (9) discussed the disappearance of experimentally deposited amyloid. He thought that there were two fundamental processes by which amyloid was removed; namely, phagocytosis and enzymotic destruction. Morgenstern (10) later described granuloma formation with giant cells and endothelial participation in the removal of experimental amyloid. In 1928, Walker (11) reported the apparent cure of amyloidosis after recovery from a chronic empyema. The enlarged liver and spleen receded, but no other evidences of cure were recorded. Waldenström (12) in the same year, reported a series of cases of bone and joint tuberculosis in which he fol-

lowed the course of the amyloidosis by punch biopsies of the liver. He found at least three cases that seemed to have recovered after surgical cure of the suppurating focus and demonstrated clearly that punch specimens taken from the liver no longer showed amyloid in regions in which it had been present previously in considerable amounts. Waldenström's cases were not studied with Congo-red dye. On the basis of pathological studies of a patient with a clinical "cure" of amyloidosis Métraux (13) concluded that resorption in the liver and kidney was accompanied by scarring, whereas restitutio ad integrum occurred in the spleen. Métraux also pointed out that anatomical evidences of amyloid
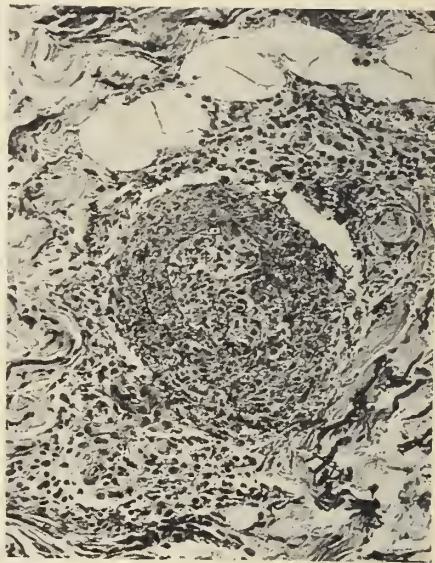
Fig. 1   Fig. 2

Fig. 1. Artery with cellular infiltration of the wall and narrowing of the lumen
    Fig. 2. Elastica stain showing periarterial and mural cell infiltration with destruction of the external and internal elastic lamellae and striking intimal thickening.

deposit could be found even after the Bennhold test had become negative and the urine had become free of albumin. In 1931 Arndt and Doerken (14) reported the frequent occurrence of amyloidosis in horses which had been used for the preparation of therapeutic sera. This observation had apparently been made earlier (15). The following year Whitbeck (16) suggested the use of liver extract in clinical amyloidosis and Grayzel, Jacobi and Warshall (17) found that liver aided resorption of experimental amyloidosis in mice. They concluded that only recently deposited amyloid was capable of resorption. Habein (18) reported a case observed at the Mayo Clinic in 1934 that seemed to indicate a clinical cure of amyloidosis after the spontaneous healing of suppurating cervical glands.

Kennedy (19) recorded a case of amyloidosis associated with chronic arthritis that apparently was cured by liver therapy. The blood pressure dropped from 200 systolic and 120 diastolic to 108 systolic and 70 diastolic, the edema disappeared, the albuminuria almost cleared up and the Congo-red retention dropped from 74 per cent to 27 per cent. Another apparent cure of amyloidosis secondary to chronic empyema was published by Reimann (20) in 1935. Moschcowitz (21) published an excellent review in 1936 and stressed the clinical aspects of the condition. Rosenblatt (22) observed a tuberculous patient with a Congo-red absorption of 100 per cent who improved and in two years only 10 per cent of the dye was absorbed from the blood stream. In 1936 Elkund and Reimann (23) found a high serum globulin in the experimental amyloidosis of rabbits caused by injections of sodium caseinate and suggested that this hyperglobulinemia was the primary factor in the causation of amyloidosis. Somewhat similar concepts had already been promulgated by Kuczynski (8) and Letterer (24).

A fatal case of periarteritis nodosa in a woman with lues was reported by Volland (25) and considerable amyloid was found at post mortem in the blood vessels, cardiac musculature and lymph nodes,—the picture of so-called atypical amyloidosis.

We are presenting a case that we have observed for more than six years, a patient who presented a most unusual clinical picture, and in whom the diagnosis of generalized amyloidosis seemed certain. At the present time the patient is quite well and all clinical and laboratory evidences of amyloid disease have disappeared.

Case Report

History. At the age of seventeen, in 1927, the patient began to complain of aches in his lower extremities. These pains spread to involve his entire body. He was then confined to bed at home where he remained three months. He was later admitted to a local hospital and remained there for six months. Soon after his admission to the hospital his condition became aggravated. He had more or less continuous fever, numerous chills with temperatures as high as 106°F. and "such pain and tenderness all over his body that the bed could not be touched." After almost five months the fever subsided and the pains became less severe. Upon discharge, his knees and elbows were fixed in semi-flexion and he was told that he was suffering from "arthritis."

One week later he entered an orthopedic hospital where the contractures were overcome under anesthesia and the extremities placed in plaster casts. After several intravenous injections of foreign protein, followed by chills and fever, he was greatly improved, so that he could be discharged after four months. At that time X-ray studies revealed evidences of a generalized arthritis with some areas of bony atrophy.

The patient remained quite well for almost three years, or from March 1928 to February 1931.

In February 1931 he developed severe pain in the back of his neck and vomited. Within twenty-four hours joint and bone pains reappeared. The patient became comatose and was again hospitalized. He was seen by Dr. J. J. Wiener. Shortly thereafter a generalized eruption appeared which consisted of soft papules which quickly ulcerated and coalesced, forming large ulcerated areas which healed, leaving deep scars. The lesions appeared in crops all over his skin, some areas healing, while new areas of ulcerations developed. The mucous membranes were not involved, but a large perforation developed in his nasal septum after rather insignificant trauma (picking) to his nose. The tips of the right

Fig. 3. Photograph of the patient taken in August 1931 when his weight was down to 85 pounds, 9 ounces. It shows numerous, deep and extensive ulcers on his arm, trunk and leg on the right side, and the left index finger which was the site of spontaneous amputation of part of the terminal phalanx. The left arm, leg and trunk were similarly involved.

and left forefingers became gangrenous and the distal phalanx of the left forefinger sloughed off.

In August 1931 he was transferred to the Montefiore Hospital, where we saw him for the first time. At that time he weighed 85 pounds, 9 ounces, having declined from his normal weight of 146 pounds (see figure 3). He was hospitalized for ten months and during that period all his symptoms gradually subsided. Various ulcerated skin lesions appeared and healed, leaving deep scars. He had an episode of stupor lasting two weeks, several convulsions and a toxic exhaustion psychosis. His liver enlarged, and it is significant that two Congo-red tests revealed tissue retention of 90 and 100 per cent respectively during this period of hospitalization, which lasted from August 15, 1931 to June 2, 1932. The

diagnosis of amyloidosis was made. The skin lesion was considered to be an unusual form of erythema multiforme.

The patient did fairly well after his discharge from Montefiore Hospital until late in February 1934, when he "caught cold" and had a sore throat. These symptoms subsided and he was well for one week. He then noted pain and tenderness over his joints and muscles and soon thereafter a blotchy eruption appeared on his right arm and forearm. Directly after the appearance of the eruption he.became febrile and was admitted to The Mount Sinai Hospital on March 12, 1934.

Examination. At that time his temperature was 103°F. and he was acutely ill. There were pain and tenderness in most of the larger joints. A generalized, but slight lymphadenopathy was found. The septal perforation was still present. The heart and lungs were normal and the blood pressure was 130 systolic and 80 diastolic. The absence of the terminal phalanx of the left forefinger was noted. The ocular fundi were normal, as was the neurological status. The skin was most unusual. There were numerous large and small deep scars over the entire body, particularly the lower extremities. These scarred areas were covered by thin, parchment-like skin with telangiectatic areas. There were also recent lesions consisting of slightly raised erythematous nodules with a deep-purplish center varying in size from 2 to 4 cm. in diameter. These were tender, painful, and often confluent. After several days bullous centers developed in them and many broke down, leaving ulcerated areas.

Laboratory Data. Cultures from the blebs remained sterile. On admission the blood count revealed: hemoglobin, 72 per cent; white blood cells, 25,900; polymorphonuclear cells, 87 per cent; lymphocytes, 12 per cent; and monocytes, 1 per cent. The von Pirquet reaction was negative. The sedimentation time was eight minutes.

On March 20, 1934 an inguinal node was removed for pathological study and culture. The gland was sterile and revealed only evidence of acute lymphadenitis on section.

Course. The patient continued to run a febrile course and new crops of skin lesions would appear. Some of these subsided and others developed bullous centers and often broke down, leaving ulcers which occasionally were confluent and healed, forming scars with circinate borders. The leucocytosis continued almost unchanged until June 1934. At that time his temperature gradually reached normal and remained normal until his discharge on August 25, 1934.

During the first month of his hospital stay there were migrating arthralgias, and about the middle of April an effusion developed in his right knee. This was not aspirated and gradually subsided. Later in April a similar painful effusion developed in the right wrist and late in May he suffered from painful effusions in his right and left knee joints.

As late as June 22, 1934 new skin lesions were appearing and becoming

ulcerated.   On July 28 he developed a venous thrombosis in his lower left abdominal wall and on August 11 several new indurated erythematous nodules appeared on his abdominal wall, although he had been afebrile for about ten weeks.

By March 25, 1934 the patient's spleen had become palpable and it remained so throughout his hospital stay.   On May 9 it was noted that his liver was definitely enlarged, confirming the clinical impression that a generalized amyloidosis existed.

The conclusion that he was suffering from a visceral amyloidosis was confirmed by the fact that by the middle of April his urine boiled solid, due to the presence of albumin, whereas it had shown only traces of this substance on admission.   On April 19 a Congo-red test was done and again 100 per cent of the dye was retained in the tissues.   On the same date a urine concentration test was done and the highest specific gravity recorded was 1008.   Further concentration tests also revealed renal damage, and at no time could he excrete urine of a higher specific gravity than 1012.   The blood urea was normal.   The blood calcium was 11 mgm. per cent; the blood cholesterol was 220 mgm. per cent of which 105 mgm. per cent were cholesterol esters.   The blood proteins were normal.   On July 21, 1934 the Bennhold test was repeated and once again 100 per cent of the dye was retained in the tissues.   On discharge on August 25, 1934 the urine still contained 4 plus albumin.   The Wassermann test and several blood cultures were negative.   During the first half of his hospital stay the patient's hemoglobin dropped from 72 per cent to 40 per cent. He received several transfusions of citrated blood and upon his discharge his hemoglobin had reached 82 per cent and the leucocytes had returned to normal (7,700).

On April 24, 1934 a biopsy was performed and a piece of skin in the left pectoral region was excised (see figures 1 and 2).   Drs. Klemperer and Otani made the diagnosis of *acute panarteritis of the skin*.   In describing figure one they report "the epidermis is without change.   The papillary body shows edema around the capillaries and slight infiltration with polymorphonuclear leucocytes, plasma cells and lymphocytes.   The vessels within the deeper corium are surrounded by a mantle of cells among which polymorphonuclear leucocytes and mononuclear adventitia cells are the most conspicuous elements."   In figure two "an elastica stain of one of these vessels (an artery) next to a group of sweat glands shows that the wall of a small artery is diffusely infiltrated, the elastic lamellae are extensively destroyed, the intima is proliferated and the lumen almost obliterated."

Second Admission.   The patient was discharged on August 25, 1934 and was well until November 23, 1934, when he was readmitted in order to have a tonsillectomy performed because each exacerbation had been preceded by a sore throat.   At that time his blood pressure had risen to

145 systolic and 100 diastolic and the urine still contained considerable albumin. The spleen and liver were still palpable. No amyloid deposits were found in the excised tonsils.

Third Admission. He was admitted to the hospital for the third time on January 22, 1935 because of an infection of one toe. There were no evidences of any active skin lesions. The liver could no longer be felt, although the spleen was still palpable. His hemoglobin was now 90 per cent and the patient was in excellent health. His blood pressure was still slightly elevated to 135 systolic and 90 diastolic, the urine showed a trace of albumin, but 100 per cent of the Congo-red was still retained by the tissues on two separate occasions. In addition to the decrease in the intensity of the albuminuria, another evidence of improved renal function was the fact that he could now concentrate his urine to 1028, whereas on his first admission complete isosthenuria existed. The infection of the toe subsided completely after simple measures were used and the patient was discharged on February 9, 1935.

Follow-Up Studies. Since his hospital discharge the patient has been seen at very frequent intervals in the follow-up clinic. His condition has remained very satisfactory. The skin ulcerations have never recurred, and he has improved to such an extent that he now does a full day's work as a waiter in a restaurant. Beginning in December 1935 he has received injections of liver extract in an attempt to hasten the disappearance of the amyloidosis. His urine has become entirely free of albumin, and his blood pressure has returned to a normal level of 125 systolic and 80 diastolic. On February 10, 1936, 54 per cent of the Congo-red was retained in the tissues. On April 21, 1937, 40 per cent was retained, and the last determination which was done on November 8, 1937 showed a retention of only 20 per cent of Congo-red in the tissues after a period of one hour. This value is definitely within normal limits. At the last examination the patient's liver and spleen were no longer palpable.

COMMENT

In searching through the medical literature there is one case which closely resembles the one described in this presentation. This is a case reported by Löhe and Rosenfeld (26). It was a case of multiple skin gangrene complicated by periarteritis nodosa in a male patient, forty-three years of age. Although a large spleen and a large liver are described in the physical examination, and there was an albuminuria, it is impossible to state whether there was amyloidosis, as the Bennhold test was not made. In this case also there was a so-called gout in both hands for many years. The case is remarkable for the multiplicity of the skin lesions (over sixty) and their extent and localization. In addition, areas of necrosis were found in the mucous membranes. As in our case, there was some question whether the condition was not due to an artefact

intentionally induced by the patient, but this was excluded by the location of some of the areas, for example, one on the larynx, and by the presence of Kaposi's sign,—that is, the deep necrotic portions of the skin were seen through the intact vesicular roof. Löhe and Rosenfeld mention that in artificial gangrene the pathologic process extends from the external layers of the skin inward, whereas the histological examination in their case revealed that the direction of the process was from within outward. The diagnosis of periarteritis nodosa in their case was made by a biopsy of the skin which revealed primary inflammatory disease of the walls of the vessels, which led to thromboses and hemorrhagic infarcts. They considered the chronic preceding infectious arthritis as the etiological factor which resulted in the periarteritis nodosa. Their case recovered after a recurring erysipelas, followed by a polyneuritis. At the final physical examination which they report, there were still some neurological changes due to the polyneuritis.

There is another case, published by Barker and Baker (27) from the Mayo Clinic under the title of "Proliferative Intimitis of Small Arteries and Veins Associated with Peripheral Neuritis, Livedo Reticularis, and Recurring Necrotic Ulcers of the Skin". This case occurred in a young man of thirty-six, who for ten years had suffered from livedo reticularis of the extremities and lower trunk, and from a series of ulcers of the legs. These had become so painful that the patient had insisted on an amputation of the leg, which was the seat of a large intractable ulcer. He suffered from acute arterial occlusion of the toes, but there was no definite gangrene. A lumbar sympathectomy gave only temporary relief from the ulcers. The pathological examination showed "a proliferative occlusive intimitis of the small blood vessels, both arteries and veins, and of larger superficial veins. The pathological picture was distinctly different from that of thrombo-angiitis obliterans, arteriosclerosis or periarteritis nodosa. There was no evidence of syphilis, tuberculosis or of any other systemic or focal infection. The etiology of the condition could not be determined, although it was thought that possibly an episode of lead poisoning four years *after* the onset of the disease had contributed to the changes in the blood vessels and nerves. This remarkable case is probably of a different character from the one published by Löhe and Rosenfeld and by ourselves.

There is another case, published in 1926 by Sézary, Hillemand and Laurent (28), which has a certain resemblance to the cases already mentioned, but again is not identical. This was a woman, seventy years of age, who suffered from a non-diabetic dry gangrene of the skin associated with a gangrene of the extremities. She also had had an arthritis of ten years' standing of the large and of most of the small joints. For the previous six years she had suffered from pruriginous crises and for the previous two years had small ulcers on her right knee and leg which

resembled mal perforant. At the examination they found a gangrene of the large toe and skin lesions on the arms, face, thighs and breasts. There were about ten areas, which varied from the size of a five franc piece to a small plate, which were hyperesthetic and not infiltrated. In three weeks' time the foci increased to twenty, some of which disappeared, others tended to become necrotic. Through treatment with insulin (although the patient was not diabetic) there was a marked improvement and almost a cure of the condition.

SUMMARY

A case is herewith reported of multiple gangrene of the skin associated with a panarteritis of the skin, as revealed by biopsy. The cause of this vascular change was probably toxic and infectious, and associated with a recurrent polyarthritis which had first appeared acutely ten years previously. As a result of the extensive and deep-seated gangrene of the skin with its long-standing suppuration, an amyloidosis of the liver, spleen and kidneys had occurred. This was confirmed by the Bennhold test. Possibly as the result of liver therapy and of the high vitamin diet, the evidence of amyloidosis gradually disappeared. The enlargement of the liver and spleen was no longer demonstrable, the albuminuria disappeared, and the Bennhold test, which had originally revealed 100 per cent retention of the dye, finally showed only 20 per cent retention, which is well within normal limits.

Gruber has maintained, and his theory has been accepted by several other authors, that periarteritis nodosa is an allergic vascular reaction resulting from a great variety of toxic processes, among which infectious polyarthritis may certainly be included. It is possible that the polyarthritis and arteritis were due in our case to a common cause, or that the polyarthritis was primary, and, as a result of this infection, an arteritis of the skin occurred which resulted in extensive and deep necrotic lesions of the skin. It is extremely interesting to note that the secondary amyloidosis of the organs was a reversible process, and although such regression is well known, it has been rare in our experience to find such a dramatic recovery.

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THE MECHANISM AND TREATMENT OF PARTIAL URINARY INCONTINENCE IN WOMEN

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Among patients admitted to a gynecological service, urinary incontinence is a frequent complaint. Taylor and Watt found that of one thousand and six consecutive admissions to the Gynecological Service of the Roosevelt Hospital, 21.6 per cent suffered from it. The frequency is greater in cases requiring vaginal plastic procedures. Thus, B. P. Watson found that 66.1 per cent of one hundred and eighty-three cases of cystocele also complained of incontinence. In our series of two hundred and sixty-four consecutive cases who entered for plastic repair, 37.8 per cent were incontinent on admission.

Urinary incontinence in the female may be produced by a variety of causes. Among these must be included vesico-vaginal fistula, local congenital anomalies, including organic and functional diseases of the nervous system, such as spina bifida, and psychogenic disturbances. The present paper is concerned with the most frequent variety, namely, "stress incontinence," or what Bonney refers to as diurnal incontinence.

There are certain features observed in this group—clinical, anatomical and physiological—which must be understood before a rational therapeutic procedure can be advanced.

CLINICAL OBSERVATIONS

The *parity* of the patient is significant. Of the two hundred and sixty-four cases admitted for plastic procedures the distribution was as follows:

Gravidity	Number of Patients	Number incontinent	% incontinent
1	27	6	22.2
2	64	21	32.8
3	65	29	44.6
4	50	20	40.6
5	21	9	42.0
6	16	5	31.2
7	10	6	60.0
8	4	3	75.0

One woman who had borne ten children was continent. Another who had borne 15 children was incontinent. We have not seen any cases of stress incontinence in nullipara. Cases of this type have been mentioned by

both Furniss and Kennedy. Their occurrence is undoubtedly rare and is not easily accounted for.

On the basis of time elapsed between the last parturition and the onset of the incontinence, we distinguish incontinence beginning almost immediately after long labor from incontinence beginning after an interval of several years. In a series of one hundred consecutive cases fourteen belonged to the first group. The seventy-six cases of the second group gave a history of freedom from incontinence from one to thirty years after parturition.

Time of onset of incontinence with relation to the last parturition:

		Cases
(A)	Immediately	14
(B)	Up to 5 years	29
	6–10 years	13
	11–15 years	10
	16–20 years	9
	21–25 years	2
	26–30 years	1
(C)	Time not mentioned	22

The reasons for the delayed onset are not obvious, but it is not unlikely that the intrinsic pathology varies appreciably in the two groups.

The usual *pelvic examination* elicits no uniform findings. Although some degree of pelvic relaxation is commonly observed, there may be no gross abnormalities. In our cases 12 per cent had no evident relaxation, 3 per cent had only a cystocele, 59 per cent had both a cystocele and rectocele, and 26 per cent had cystocele, rectocele and some degree of uterine prolapse. Incontinence is rare in complete procidentia. Usually these patients complain of difficulty in initiating the stream and must often replace the prolapsed uterus before voiding is possible. A common but by no means universal finding (Bonney) is a urethra detached from its normal high fixation to the pubis, so that on straining it rotates under the pubic arch with its meatus pointing upwards to the clitoris.

Furthermore, *stress incontinence* has been known to occur for the first time in patients following very satisfactory repairs for cystocele. Ten of our cases who had a satisfactory result from the anterior colporrhaphy, first complained of incontinence after the plastic operation. Experience has shown that the results from operation for the relief of incontinence are poorer where there are no visible signs of pelvic relaxation than when a cystocele is present. The classification of incontinence according to its association with cystocele, and without cystocele, may be convenient but is somewhat misleading since it suggests two different causes for the incontinence.

Symptoms. The milder cases complain of loss of urine only on severe cough or sneezing. At first the incontinence may be present only for short periods of time, with long remissions. However, it is apt to be slowly

progressive and the severe cases may be continent only when lying in the prone position. Furniss' subgrouping is useful as an index of severity of the ailment and as a gauge in the estimation of relative operative success:

Mild—where occasional incontinence follows coughing, sneezing, etc.
Moderate—where incontinence occurs on any strain or exertion.
Marked—where incontinence occurs merely on assuming the erect position.
Complete—where incontinence occurs at all times, whether in the prone or
    erect positions.

This subgrouping carries the connotation that the same intrinsic mechanism is responsible for the four classes which vary only in degree of disability.

THE ANATOMY OF THE SPHINCTERS

A brief review of the anatomy of the sphincter mechanism is important. Most of the studies have been performed upon males and the question has been raised as to whether the anatomy of the female bladder neck is exactly similar. Two major anatomical structures are known to exist: an internal sphincter and an external or voluntary sphincter. Wesson in his microscopic studies of the vesical neck in the male describes the internal sphincter as consisting of two loops of smooth muscle. The inner loop arises from the circular layer of bladder musculature and swings downward and forward in an oblique form to about the level of the verumontanum where it loops around the front of the urethra. The outer loop is thicker and arises from the longitudinal layer of bladder musculature and sweeps over the vesical orifice. The resultant effect is not a circular sphincter but two arcuate muscle bands.

In the female this arrangement has not been demonstrated. Van Duzen and Looney found that the internal sphincter consisted of two portions: an inner and an outer. Of the inner bundle the most internal fibers form a complete circular sphincter about the internal orifice of the urethra. The outer portion of the inner bundle is similar to what Wesson described as the loop arising from the circular fibers of the bladder wall. The outer bundle is continuous with the longitudinal fibers of the bladder wall and passes on each side of the urethral orifice to the anterior surface of the urethra. Some of these muscle fibers loop around to the opposite side while others are continued into the urethral wall. Kennedy assumes that the fibers of the internal sphincter are arranged in circular fashion but offers no microscopic evidence.

The voluntary or external sphincter has been incompletely studied in the female. All observers have agreed that there are transverse fibers running largely underneath the urethra and a few above it to form a distinct muscle sling. Some of these fibers interdigitate across the median line and some terminate freely into the anterior vaginal wall. Difference

of opinion has been expressed as to the lateral origin of this muscle. H. W. Johnston claimed the origin of these fibers to be from the symphysis pubis and descending ramus on each side. Van Duzen and Looney describe this muscle as lying between the two layers of the urogenital diaphragm arising from the pubic arch on each side as well as the deep transverse perineal muscle. Kennedy and Davies claim "these fibers to be the anterior portions of the levator muscles," arising from the anterior end of the "white" line and passing under the inner third of the urethra.

Our own anatomical studies on nulliparous cadavers agree with the findings of Kennedy and Davies. We found the external sphincter to consist of a definite thick muscle bundle which at its widest portion may be a centimeter in diameter. It arises from the "white" line adjacent to the levator and passes across the median line to interdigitate with fibers on the other side beneath the upper half of the urethra. At its origin it blends directly with the levator muscle and some of the levator fibers seem to pass directly into it. Microscopic studies suggest that it consists largely of smooth muscle. This anatomical relationship of the external sphincter to the levators is important from the viewpoint of understanding the mechanism involved in the "restraint of urine" and various degrees of incontinence.

The urethral musculature itself is exceedingly scanty and consists of an inner longitudinal layer and an outer circular layer. Its fibers blend with those of the internal sphincter.

The trigonal muscle arises in the region of the ureteric orifices and swings forward along the floor of the vesical neck to end over the posterior aspect of the urethra. In 1918 Young demonstrated that this muscle passed in the form of a bow through the arcuate muscles which comprise the internal sphincter. Direct observation and pharmacologic studies indicated that by its pull the internal sphincter was actively forced open. We have been able to demonstrate the power of this muscle in a patient with complete procidentia. With the aid of a cystoscope the site of the interureteric bar was marked on the vaginal wall. The prolapse was drawn out completely and the patient was asked to void. A definite latent period occurred before the stream passed through the urethra. During this interval a crease appeared in the vaginal mucosa at the site of the interureteric bar which gradually deepened and the bladder base was drawn into the vagina along this crease before the actual stream was passed. We inferred that in this case of long-standing prolapse, in which the patient had a long history of difficulty in initiating the stream, the trigonal muscle was greatly hypertrophied and actually drew the bladder back into the vagina.

THE CLOSING MECHANISM OF THE BLADDER

In order to get an idea of the closing mechanism of the bladder numerous roentgenograms and dynamic studies were made on normal women and

those complaining of stress incontinence.   These findings were correlated with the pathology seen at operation and later checked by studies in the follow-up of the same patients.

Following the suggestion of Stevens *et al.*, cystograms were taken using routinely 250 c.c. of 10 per cent sodium iodide; this is well tolerated by the bladder and gives excellent shadows.   After the fluid was introduced, a fine metal chain was passed through the urethra into the bladder so that at least four inches of chain lay within the bladder to provide against

Fig. 1. Case J. L.—gravida II, para II—no incontinence and no cystocele.   Films taken in the oblique position with chain in situ in bladder and urethra.   *A*. Resting film.   *B*. Straining film; no funnelling is visible.   *C*. Voiding film.   *D*. Double exposure, indicating slight descent of the urethra but no funnelling on straining.

premature extrusion during the straining effort on the part of the patient. The urethral meatus is best marked by a Michel clip.   In our earlier work we used a metal guide held by the operator but this is apt to be quite unsteady.   In some cases it is also of value to place another clip at the anterior cervico-vaginal junction and a third on the vaginal wall at the site of the vesical neck.   The most useful information is gained by taking roentgenograms in the oblique position.   For each position four plates were taken: (1) exposure of the full bladder at rest, (2) with patient instructed to strain down forcibly but at the same time to "hold" the

flow, (3) a double exposure taken with the patient "holding" and then straining but "holding," (4) during voiding. The chain outlines the urethra during the act of voiding, requiring no contrast filling from the outside with iodized oil. Particular attention was paid to the bladder neck, the descent of the urethra during straining, and any changes in the urethral contour during voiding (Figures 1 to 6).

The action of the internal sphincter in the male has been beautifully demonstrated by the physiologic studies of Denny-Brown and Robertson. They confirm the work of Rehfisch that there is a physiologic closing

Fig. 2. Case B. F.—gravida IV, para IV—previous urethroplasty, recurrent incontinence with no cystocele. Films taken in oblique position with chain in situ. *A.* Resting film; no funnelling present. *B.* Straining film; marked funnelling. *C.* Double exposure; slight descent of the urethra with marked funnelling on straining.

mechanism proximal to that which is subject to voluntary control and which is identified with the internal sphincter at the neck of the bladder. They showed that the internal sphincter could not be induced to open without the presence of an active vesical contraction. Passive increase of intravesical pressure by introducing large volumes of fluid failed to render the sphincter patent. They supported the thesis of Young and Macht that during voiding the internal sphincter is actively forced open by the trigonal muscle. The strength of the internal sphincter in the male is quite considerable and, if called upon, it alone may preserve continence.

This was first shown experimentally by Rehfisch who passed a catheter in a male so that its end lay between the internal and external sphincters. On straining no fluid passed through the catheter. This was further demonstrated clinically by many continent patients whose voluntary sphincters have been destroyed through perineal prostatectomy or trauma.

In our X-ray studies of normal women, no funneling of the bladder neck was seen during straining at a time when the intravesical pressures reached 100 mm. of mercury or more (Fig. 1). Rehfisch's procedure was
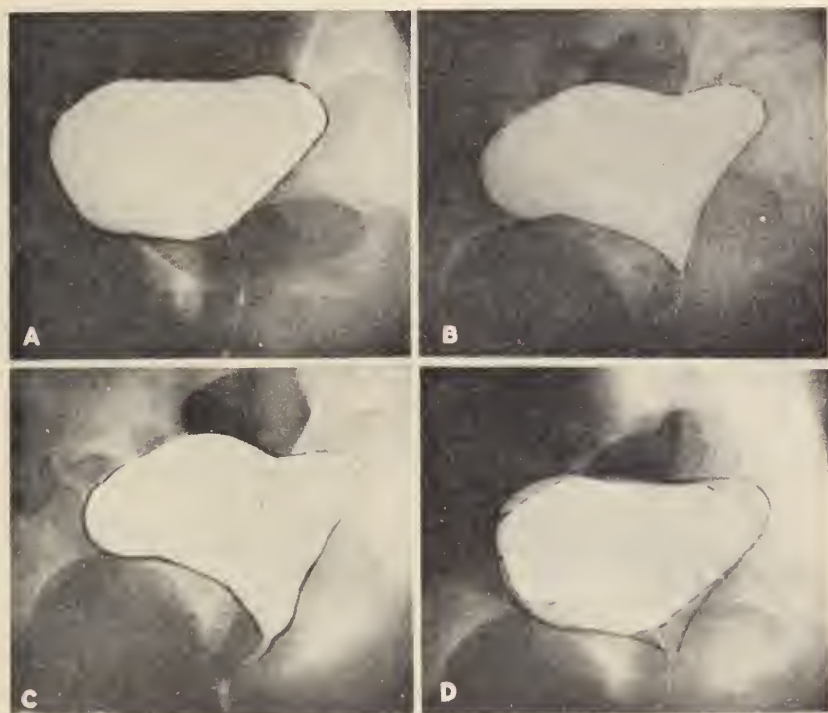
FIG. 3. Case M. H.—gravida IV, para III—prolapse of the cervical stump following supracervical hysterectomy, incontinence with cystocele. Films taken in oblique position with chain in situ. *A*. Resting film; no funnelling. *B*. Straining film; marked funnelling. *C*. Voiding film. *D*. Double exposure; marked funnelling and slight descent of the urethra on straining.

performed on the female with similar findings. A steel open-end catheter could be passed to a point only 3-4 mm. from the internal urethral orifice without leakage of urine despite the fact that the patient was straining forcibly.

The action of the external sphincter is difficult to demonstrate in the female, whereas in the male studies are quite easily made because an appreciable distance separates the two sphincters. By keeping the internal sphincter open with a special instrument Young has shown in the male that perfect continence can be maintained by tonic activity

of only the voluntary or external sphincter. Urethrograms taken on continent patients following suprapubic prostatectomy have often demonstrated the internal sphincter to be widely dilated, while adequate continence is maintained at the level of the voluntary sphincter.

Attempts have been made to measure numerically the actual strength of each of the two sphincters. Simons described a sphincterometer consisting of a small rubber bag at the end of a catheter which he connected to a manometer and a source of fluid supply. The bag is passed so that

Fig. 4. Case B. H.—gravida VI, para III—marked prolapse with cystocele; no incontinence. *A*. Straining film; marked descent of base of bladder without funnelling. *B*. Double exposure: marked descent of base of bladder without funnelling on straining, some descent of urethra. *C*. Resting film.

it is embraced by either the internal or external sphincter and is then filled with the predetermined amount of fluid which would dilate it to the size of a #47-Charriere. A reading is then taken on the manometer with that amount of fluid in the system. He found the tonus of the internal sphincter to average 13 mm. of mercury and the external sphincter 19 mm. of mercury. However, this method is open to question on two points: (1) the bag shown by X-ray to be grasped by the internal sphincter is also of necessity partially in the bladder and so reflects intravesical

pressure as well; (2) the method does not permit the determination of the tonus of the sphincter at various levels of intravesical pressure. Further-
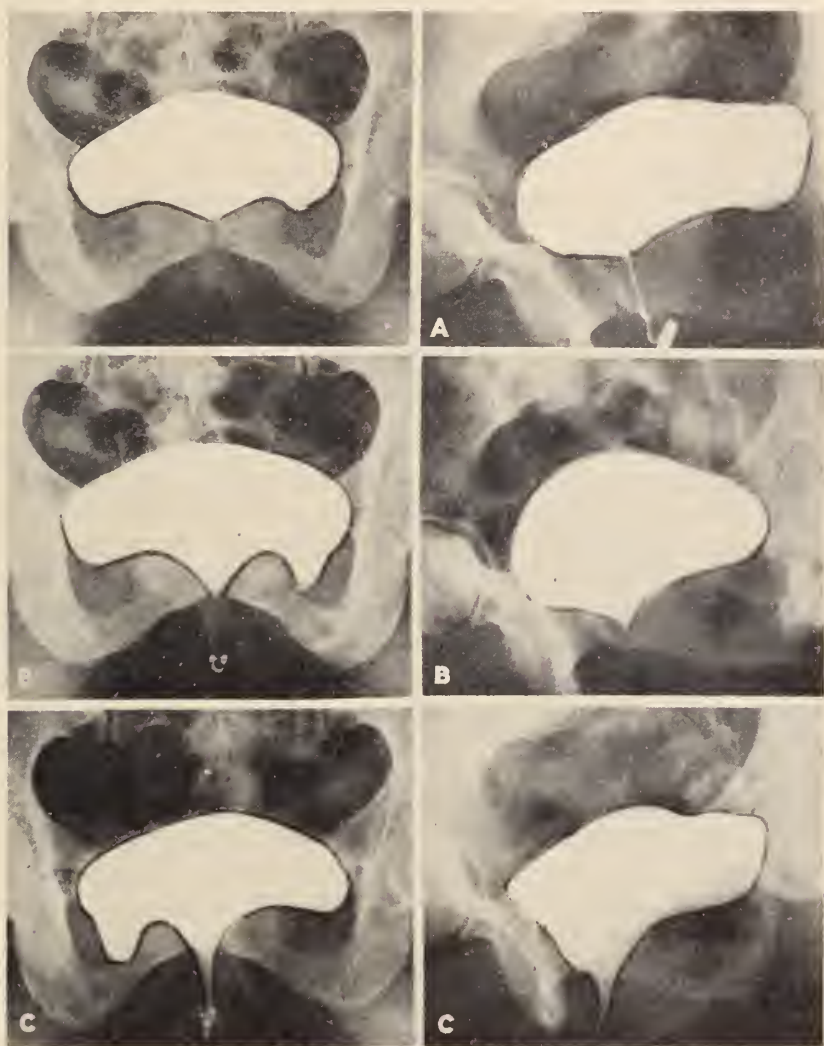
Fig. 5. Case H. H.—gravida I, para I—previous urethroplasty, recurrence of incontinence without cystocele (A-P exposures). *A.* Resting film; funnelling on passive distention of bladder. *B.* Straining film; funnelling increased. *C.* Voiding film; metallic clip marks external urethral meatus.

Fig. 6. Case H. H. Same case as Figure 5; films in oblique position. *A.* Resting film; slight funnelling. *B.* Straining film; funnelling increased. *C.* Voiding film.

more, the catheter and the bag splint the urethra and possibly impair the action of the sphincter.

Kennedy introduced a bag which lay partially in the urethra and par-

tially in the bladder. By increasing the quantity of fluid in it and using a manometer he determined the pressure required to cause funneling.

Both of these methods are more or less direct measurements in the sense that the pressure exerted on the sphincter comes from within the lumen of the sphincter and urethra. Inasmuch as the sphincter must resist a pressure directed against it from the bladder, it has seemed to us that indirect measures might give more accurate and clinically perhaps more valuable findings. A small balloon filled with fluid was introduced into the rectum and attached to a manometer. We found the intra-rectal pressure to parallel exactly the intra-vesical pressure *during either straining or when the abdomen was pressed upon by the observer.* The following conclusions were reached: (1) the intra-rectal pressure rises at the most a few millimeters of mercury during the passive filling of the bladder with a quantity of fluid which raises the intra-vesical pressure to 30 to 40 mm. of mercury. (2) During actual voiding the intra-rectal pressure rises 10 to 12 mm. of mercury when the patient is in the prone position and only 3 to 4 mm. of mercury while erect. As has been previously shown, voiding is produced by active contraction of the bladder itself and does not demand abdominal wall contraction. There is definite relaxation of the pelvic floor during micturition and contraction of the pelvic muscles when the patient attempts to "hold" the urinary stream. (3) Contraction of the perineal muscles associated with the effort of "holding" raises the intra-rectal pressure about 5 mm. of mercury. A cough of mild intensity raises the intra-rectal tension about 10 mm .of mercury, but strong forced coughs caused a rise to as much as 50 mm. of mercury. (4) The intra-rectal pressures were determined at the occurrence of incontinence under two further conditions: (a) when the patient strained without "holding" and (b) when she bore down and consciously attempted to control the urinary stream. We found that regardless of the quantity of fluid in the bladder, incontinence occurred at only a definite intra-rectal, i.e., intra-vesical, threshold of pressure. In all our cases incontinence occurred at much lower pressures when no attempt was made to "hold." However, the difference between the two thresholds becomes much smaller when the patient assumes the erect position. Patients volunteer the information that "holding" is mechanically more difficult when erect than in the prone position. We believe that the maximum amount of intra-vesical pressure that the patient can reach by straining but "holding" before incontinence supervenes forms a useful index of the relative strength of the voluntary sphincter. The threshold reached during straining without "holding" is determined by the tonus of the internal sphincter in addition to the "subconscious" assistance rendered by the voluntary sphincter (Fig. 7).

Other factors besides a sphincteric action have been considered as playing a rôle in the restraint of the urinary stream. Bonney believes

that the angle formed by the urethra and bladder at the vesical neck exert a valve-like action. His claims were based on the clinical observation
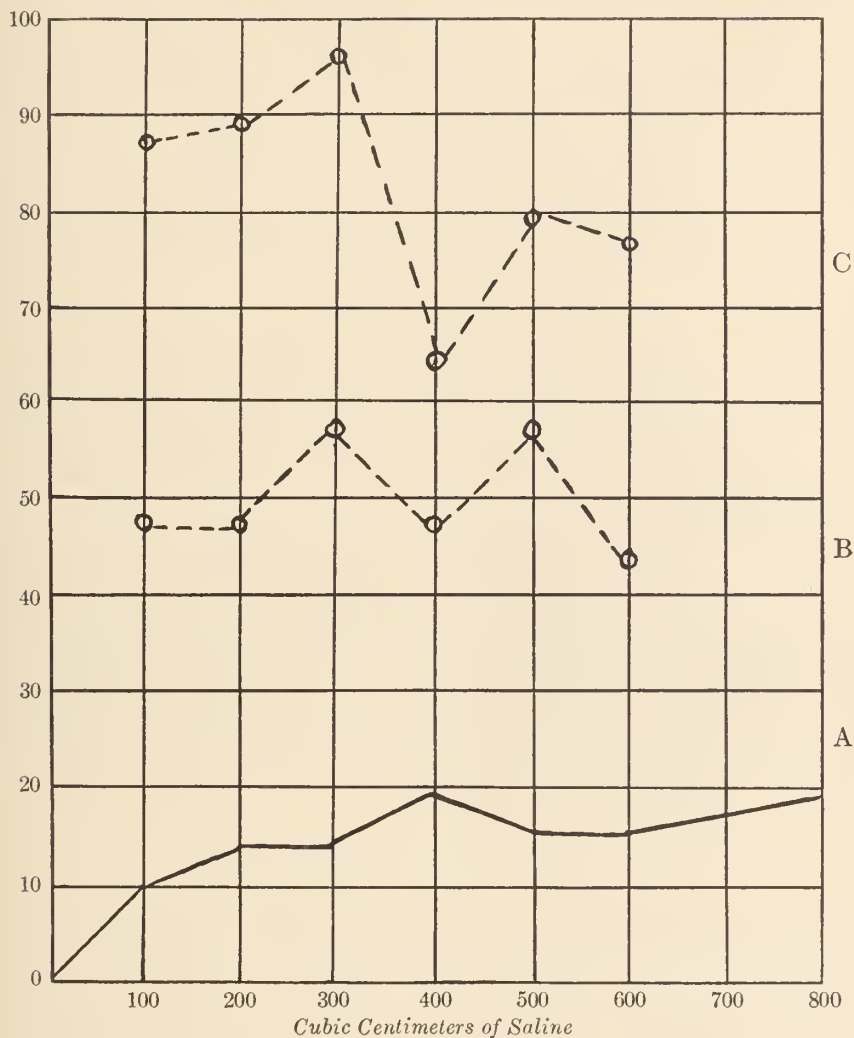
Fig. 7. Case H. H.—Dynamic studies of bladder function. Curves B and C represent pressure readings gained by means of a balloon in the rectum, recording intra-rectal, i.e. intra-vesical pressure during straining. *Curve A*—cystometric curve obtained, using a water manometer. The rise in intra-vesical pressure to passive distention with fluid produced a curve which is practically the same as we have found in continent women. *Curve B* represents the threshold of pressure at which incontinence occurred when the patient strained without 'holding' at various bladder fillings. ⊙ ⊙—points at which incontinence occurred. *Curve C* represents the threshold of pressure at which incontinence occurred when the patient strained and at the same time attempted to 'hold' at various bladder fillings.

that in patients with "stress" incontinence the urethra is usually detached from behind the pubis and descends on straining. Moreover, the infre-

quency of incontinence associated with total prolapse he ascribes to the fact that the relatively greater descent of the bladder restores the normal angle. However, we found, both clinically and by our roentgenograms, that many patients with stress incontinence had no descent of the urethra on straining and also that the converse was true. As we will show later, the descent of the urethra is merely an associated finding due to injury to the external sphincter and of itself causes no symptoms.

Natvig has claimed that the chief factor in the restraint of urine is not the sphincters but the muscles of the pelvic floor through their effect on the size of the urogenital hiatus. The perineal muscles always relax during voluntary micturition and contract with voluntary restraint. Denny-Brown and Robertson consider these as merely "associated" movements and the perineal muscles as exerting no direct effect on the closing of the bladder. However, from our dissections we have seen that the voluntary sphincter is anatomically related to the levators. Moreover, on forcibly depressing the floor of the vagina thus impairing the action of these muscles it is found that the force of the voluntary sphincter is distinctly reduced.

In summary, it is our belief that the closing mechanism of the bladder in the female rests upon a dual mechanism: one, the internal involuntary sphincter; and the other, the external voluntary sphincter which is closely associated with the levator ani, the chief muscle of the pelvic floor. In all probability, the internal sphincter can, under ordinary circumstances, alone maintain continence but under the special conditions of sudden, more or less violent increase in intra-abdominal pressure, as produced by coughing or straining, the external sphincter acts as an auxiliary agent to prevent involuntary escape of urine.

EXPLANATION OF "STRESS INCONTINENCE"

The differences of opinion as to the mechanism involved in "stress incontinence" are largely based upon the varying concepts as to the anatomy and relative importance of the sphincters and the pelvic floor which are engaged in the control of micturition. Any single theory to be completely satisfactory must reconcile all the clinical observations, the results of specific surgical treatments, and the experimental studies. The major hypotheses that have been advanced include: (1) The claim of Stoeckel and others that the incontinence is produced by actual injury to the sphincters by the trauma of labor. H. W. Johnston specifically claims the injury is one of the voluntary sphincter. (2) The theory of N. F. Miller and others that the incontinence is produced by relaxation of the sphincters and not direct injury to the muscle fibers. (3) The assumption of Bonney and B. P. Watson that "stress incontinence" is produced by laxity of the anterior musculo-fascial sheet, permitting the bladder to slip behind the symphysis with the urethral and peri-urethral

wedge carried down and forward. They claim that incontinence results from both a loss of the valve-like action of the urethro-vesical angle and the weakened 'point d'appui' for the action of the intrinsic muscle sphincters. (4) The theory of Taylor and Watt that the prolapse of the neck of the bladder and the urethra involves only its inferior part and the drag of these structures keeps the sphincter open. (5) The theory of Kennedy that "labor may injure (a) separately the voluntary sphincter by directly or indirectly causing it to be distorted and fixed to the ramus of the pubis thereby very markedly diminishing its function as a sphincter; (b) separately the voluntary sphincter by splitting its fibers parallel to the urethra in or adjacent to the median raphe; (c) conjointly at the same labor by (a) and (b)."

From our observations incontinence of any sort is probably due to incompetence of both the internal and the external sphincters. In the group occurring immediately after labor direct trauma to the muscle fibers comprising the sphincters probably constitutes the major cause. Cystoscopic examination early in the puerperium often shows a severe hemorrhagic trigonitis, indicating the amount of trauma which the passage of the fetal head may inflict upon the base of the bladder. To this same factor we attribute those cases of incontinence which first appear after the performance of a simple anterior colporrhaphy.

However, a majority of the cases and most of the clinical data are better explained by the theory of relaxation or stretching of the closing mechanisms of the bladder. At operation the voluntary sphincter is always found in a frayed and stretched-out state with most of the weakness in the suburethral area. Gross evidence of the weakness of the internal sphincter cannot be obtained. Funneling of the bladder neck on straining was found in all of our incontinent cases and in none of our continent controls. This indicates that the sphincter had been forced open by small rises in intra-vesical pressure. Normal continence has not been associated with funneling. One of our severe cases of "stress incontinence" exhibited funneling on mere passive distension of the bladder with small amounts of fluid which were associated with only small rises of intra-vesical pressure (Fig. 6). The detachment of the urethra and its marked descent during straining we interpret only as a sign of weakness of the external muscle sling which is the major support of the urethra.

A variety of factors contribute to the stretching of the sphincters. When incontinence is present the sphincters can scarcely be said to be exposed to a persistent high intra-vesical tension due to vesical hypertonicity. Routine cystometric studies on our cases of incontinence yielded curves which with few exceptions showed no difference from the findings in an equal group of cases with simple cystoceles and no incontinence (Fig. 7, A). Two cases of complete incontinence had a severe hypertonic type of curve which we attributed to the chronic contraction of a bladder

which is constantly emptied. However, as Crabtree *et al.* have shown, the intra-vesical pressure which a cystocele must develop before voiding occurs is, as a rule, higher than that of normal bladders and this added pressure strain during voiding may be significant. The weakness of the anterior vaginal wall in cases with cystocele produces a continuous drag upon the urethra, stretching the voluntary muscle sling. The descent of the bladder in these cases draws down the entire urethra and not merely the posterior wall, as suggested by Taylor and Watt. This has been proven by our urethrograms during straining and voiding. Seventeen of thirty cases of "stress incontinence" treated only by anterior colporrhaphy or by parametrial fixation without any attempted urethroplasty were cured of their incontinence. By elevating the bladder these procedures permit the voluntary sphincter which has been stretched to regain its normal tone. We have not been able to observe any adhesions between the ramus of the pubis and the involuntary sphincter and at operation the bladder neck is often excessively mobile. Definite adhesions, however, have been seen between the pubic arch and the voluntary sphincter which might possibly impair their function.

OPERATIVE TREATMENT

The number of operative procedures employed to cure incontinence has been legion. Many of them differ from each other only in the nomenclature of the tissues utilized. In his monograph Kelly summarized the earlier operative techniques and Abeshouse the more recent. We have borrowed from them some of their classification:

A. Procedures plicating the remains of the internal sphincter or the urethral walls or both, or the creation of some stenosis of the vesical neck:
  1. The injection of paraffin or sclerosing solutions per urethra has been largely employed in the nineteenth century.
  2. Frank, 1882, excised a wedge from the floor of the urethra including the underlying vaginal wall and narrowed the lumen by re-suture.
  3. Winckel, 1886, removed a wedge-shaped flap from the anterior vaginal wall down to the urethral mucosa. On re-suturing the denuded area the overlying urethral floor was imbricated.
  4. Desnos, 1890, directly exposed the upper two-thirds of the urethra and passed a series of imbricating catgut sutures.
  5. Pawlik, 1883, and Duret, 1891, advanced the urethral meatus to a point beneath the clitoris.
  6. Pousson, 1892, resected the external meatus and part of the urethra, twisted the remaining urethra 180° and transplanted it below the clitoris.
  7. Albarran, 1892, narrowed the whole urethra by imbricating sutures and transplanted it below the clitoris.
  8. Dudley, 1895, advanced the urethra without detaching it from its immediate surroundings avoiding the danger of slough through deprivation of blood supply.

9. Hackenbruch, 1909, through a suprapubic extraperitoneal approach reefed the neck of the bladder.

10. Kelly, 1913. The Kelly procedure has been the most popular repair performed in the past twenty years for "stress incontinence." He introduced a Pezzer catheter and located the region of the vesical neck. A median incision was made into the anterior vaginal wall over the urethrovesical junction and the vaginal wall was reflected laterally for a distance of 2 to 3.5 cm. Two to three mattress sutures of silk or linen were then passed. The first took about 1.5 cm. of tissue in the region of the vesical neck and the other two sutures were passed lateral to it. Redundant mucosa was excised and the vaginal flaps re-sutured.

11. Young, H., 1908, in the male, and Smith, M., 1930, in the female sutured the remains of the internal sphincter through a transvesical approach. The mucosa over the sphincter was denuded and the relaxed or torn fibers approximated with the aid of a boomerang needle-holder.

12. Furniss, 1924, through a suprapubic extraperitoneal approach reefed the bladder neck and anchored the imbricating suture to the fascia of the anterior abdominal wall to elevate the urethro-vesical junction. He employed this technique only in cases where the Kelly operation was inadvisable.

13. Lowsley, 1928, excised a wedge from the anterior wall of the urethra and vesical neck. In 1936 he suggested the use of a piece of ribbon-gut tied snugly about the urethra in cases of "stress continence." The gut is eventually replaced by scar tissue.

14. Of more recent years, some scarring of the vesical neck and shortening of the internal sphincter has been effected by direct radial electro-coagulation through the endoscope.

B. Procedures strengthening the pubo-cervical muscle sheet and creating continence without presumably affecting the sphincter muscles.

Both V. Bonney and B. P. Watson in 1923 recommended the formation of a buttress by imbricating the "fascial" or muscular flaps in the anterior vaginal wall, suburethrally, and elevating the urethra.

C. Douglas' method of producing a ball-valve at the vesical neck, 1935.

By means of concentric purse-string sutures in the region of the urethro-vesical junction the sphincter is tightened and at the same time a ball of tissue is produced which encroaches on the urethral tissue.

D. Direct exposure and repair of the sphincters.

1. Young, E. L., in 1922 and Johnston, H. W., in 1931 dissect out the urethra in the region of the bladder neck, isolate the retracted fibers of the external sphincter and re-suture them beneath the urethra. Johnston claims that the virtue of the Kelly suture lies in the inadvertent catching of the external sphincter fibers in the mattress sutures.

2. Kennedy, 1937, frees the internal sphincter from adhesions to the surrounding structures, plicates the urethra in a manner so that healthy peri-urethral fascia entirely surrounds the urethra and then with silver wire catches the vaginal mucosa and retracted ends of the voluntary sphincter and the upper portions of the pubo-rectalis muscles on both sides.

Careful follow-up over a period of years taking complete continence as the sole criterion of cure in any given case has shown that the Kelly pro-

cedure in our hands has given relatively poor results. This may very well be due in part at least to failure in following Kelly's original technique. Of fifty-seven cases performed by this technique, only 36.8 per cent were cured whereas 56 per cent of thirty cases of 'stress incontinence' were cured following a parametrial fixation operation or the simple anterior colporrhaphy.

During the past year, we have attempted to determine the degree of incontinence by adopting suitable measures for each case. We have found that in the very mild cases non-operative treatment is often success-ful. The patient is instructed in the conscious effort of controlling the urinary stream and is made aware of her power to use and exercise the voluntary sphincter while she is straining or bearing down. The aim of cystometric determinations is that through their aid we may be able to formulate the type of operation that will be adequate and suitable for the degree of incontinence in each case.

In the most severe cases of incontinence some type of relief has hitherto been effected by muscle transplant. Practically every local muscle has been employed since Giordano in 1907 swung over a gracilis transplant. The rectus was first used by Giordano in 1908, the pyramidalis by Goebell (1900), the levator by Squier (1911), the adductor magnus by Borchard (1914), gluteus maximus by Sellheim (1915), a free fascial sling attached to the rectus by Price (1933), the round ligaments by Solms (1919), and the bulbocavernosae by Martius (1929).

Experience in the past with the surgical treatment of urinary incon-tinence has shown that often a successful result is achieved without know-ing exactly how it was achieved. In general, success has seemed to follow several procedures in varying percentages. Mention has already been made of cases where simple anterior colporrhaphy or parametrial fixation resulted in cure despite the fact that no specific steps were taken to combat the incontinence. However, two established procedures appeared to be based upon some logical anatomical concept and were therefore employed by us. The one was to reef in purse-string fashion or by a figure of eight stitch the musculo-fascial planes about the vesical neck or some part of the urethra after the fashion of Kelly's operation. The other was to sew the fascial muscular tissues from near the pubic ramus of one side to that of the other side and thus tighten and narrow the urethral lumen after the technique of Halban. The first method produced a spur or buttress which narrowed the urethral lumen and resulted in a ball-valve-like action. It was adopted especially for recurrent incontinence and in some cases three concentric layers of sutures were taken in order to effect a projection into the urethra. The second method secured a constricting band across the longitudinal axis of the urethral lumen. Halban has stated that this method in his hands was satisfactory for 80 per cent of his cases.

Special anatomical and clinical studies have more recently brought to

light the fact that in either case the retracted fibers of the voluntary sphincter were thus brought together at the midline. As the fibers of this muscle interdigitate laterally with the levators the latter are second-arily obliged to exert their powerful voluntary pull when there is demand for controlling the urinary stream. The voluntary sphincter is thus made taut, with the result that the urethral lumen is flattened out.

We have found that continence can be restored momentarily by placing the finger tip against any portion of the urethra. No matter how lightly the finger is thus applied it affords the patient sufficient support to enable her to control the act of urination. If one could construct a pessary which would yield this type of support, i.e., to flatten the urethral wall at any one point against the inner aspect of the symphysis it would obviate the necessity of resorting to surgery for the relief of mild and even moderate degrees of urinary incontinence. This has been found difficult and only exceptionally a pessary can be fitted which will successfully accomplish adequate support. A firm posterior vaginal wall and perineal body are essential to keep the pessary in place.

A procedure which one of the present writers* has used a number of times was designed to supply such additional support by using ox fascia which was stitched from one levator edge including the ischio-cavernosus muscle across the urethra to similar points on the other side. In several severe cases this appeared to be a decided aid. It has not been possible to tell what has actually happened to this ox fascia; whether it was re-placed by connective tissue or not cannot here be answered.

It has seemed to us that if we can utilize structures which are anatomi-cally present and which can be united across the urethra that the buttress and support expected from ox fascia would be better accomplished.

In the past year we have employed a procedure which has utilized these principles and, as in the procedure of Kennedy, has attempted to restore the integrity of the external or voluntary sphincter. The dissection is not as extensive as that employed by Kennedy nor is the urethra mobilized as widely. We have not seen adhesions as commonly but agree that where adhesions exist it is well to free the vaginal wall from the bladder, pubic rami and muscles to permit better approximation. In recurrent inconti-nence dense adhesions between the voluntary sphincter and the pubic rami may offer difficulty in dissection.

Surgical Procedure. A midline incision is made into the anterior vaginal wall from the urethral meatus to the urethro-vesical junction and some-what beyond. With a stiff catheter, ✳18F, in the urethra as a guide, the vaginal mucosa and submucosa are reflected laterally by sharp and blunt dissection to the anterior border of the pubo-rectalis muscle. The voluntary sphincter is carefully outlined and freed as far out as the pubic

* I. C. Rubin.

ramus.   It is thick and almost ligamentous in the mid-portion immediately underlying the urethra and thins out into fascial and muscular fibers as they pass out laterally.

The urethra is not mobilized extensively.   The attachments of fascial and muscular fibers to the urethral walls are not cut but are preserved as such.   This avoids bleeding which is otherwise encountered through injury to the perivesical veins and the inferior vesical artery.   A silk purse-string suture in figure of eight fashion is passed through the fascial muscular fibers of the so-called triangular ligament (external, voluntary sphincter) including the external coat of the urethra at the bladder neck or distal to it (Fig. 8).   Another similar suture is taken a centimeter to one and one-half centimeters outside of the first suture and includes in
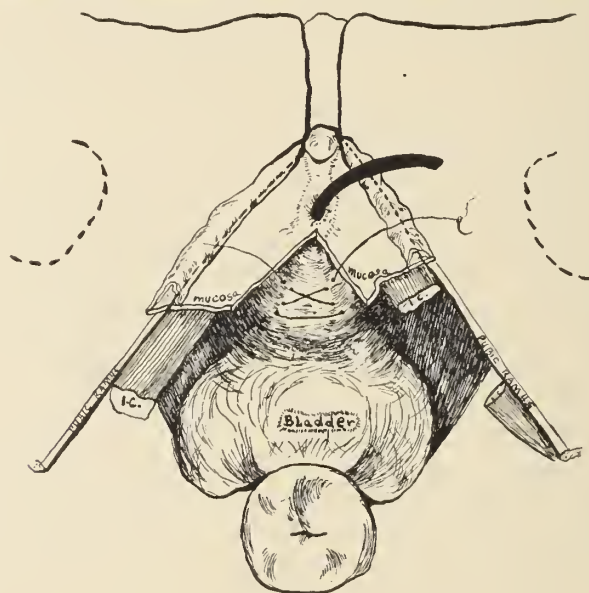
FIG. 8 (see text)

its bite the mesial fibers of the voluntary sphincter.   This has the triple effect of plicating the internal sphincter, shortening the external sphincter and producing a small ball-valve at the bladder neck.   By drawing the bladder and urethra to one side the upper end of the pubo-rectalis bundle of the levators comes distinctly to view, as well as the origin of the voluntary sphincter.   Three heavy chromic sutures or kangaroo catgut of moderate thickness are passed, catching the pubo-rectalis and the retracted fibers of the voluntary sphincter on each side, bringing them together under moderate tension in the midline (Figs. 9 and 10).   (A stay suture of kangaroo tendon or chromic catgut was next passed through the vaginal mucosa overlying these structures and through them from side to side in order to remove the tension on the underlying sutures.   As this was found
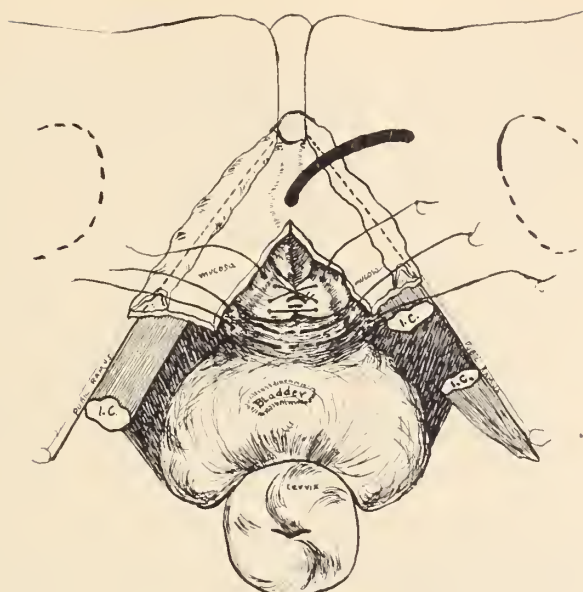
FIG. 9 (see text)
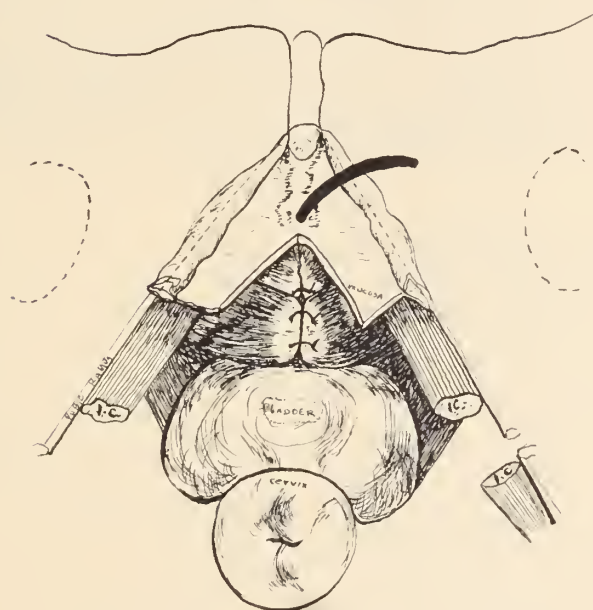
FIG. 10 (see text)

to cause necrosis and separation of the vaginal mucosa we have since dis-
pensed with it.) Redundant mucosa is excised and the flaps are re-
sutured into position. A #14F open-end catheter is passed into the

bladder and is stitched to the labium minus where it is maintained for from six to eight days.

The steps in the procedure just outlined have the advantage of utilizing the valuable features of the Kelly and the Halban techniques, in addition to which the levators are brought together in the anterior portion of the urogenital hiatus in a fashion which has been utilized in the posterior portion of the urogenital hiatus for the cure of rectocele. As in the latter case, it is not expected that a restitutio ad integrum will be accomplished by this procedure. Complete anatomical restitution is not possible, for example, in the repair of old third degree tears of the perineum where the torn ends of the sphincter ani are brought together. Nevertheless, satisfactory rectal continence is accomplished, despite the fact that the original anatomic neuromuscular arrangement is not exactly restored. In the same way the levators are brought together in the upper or anterior portion of the genital tract and are made to bear the brunt of the lost power of the urethral sphincters.

The primary results from this new procedure have been uniformly good; at least the patients have all been completely continent when they were discharged from the hospital. A few of these were cases that came in for the cure of recurrent incontinence, the failure of the first operation being evident before or at the time they were discharged from the hospital. However, the follow-up on these recent cases is as yet too inadequate to speak of lasting results. It remains to be seen whether recurrences may be noted later as have been seen after practically all other methods hitherto employed for the care of this condition in women.

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CONGENITAL POLYCYSTIC KIDNEYS WITH SECONDARY BONE CHANGES (RENAL HYPERPARATHYROIDISM; RENAL RICKETS)

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Although by this time quite a number of cases of so-called renal rickets have been described, we feel justified in reporting another case in order to emphasize the fact that within the last few years our understanding of the pathogenesis of this condition has been considerably enlarged. Cases have been reported under the name of renal infantilism, renal dwarfism, renal rickets, and many hypotheses have been put forth to link up the bone changes with disease of the kidneys. In 1928 Duken (1) advanced the theory that an endocrine factor might be involved and suggested that the parathyroid gland might be responsible for part of the pathology. This has been emphasized by others (Shelling, Jaffe, Park and Eliot (2)) so that at the present date, the interesting pathogenesis of this condition seems fairly well understood. Moreover, we felt that a report of this case was particularly appropriate in a series of papers dedicated to Dr. Edwin Beer, since the whole clinical picture depends in its final analysis on a lesion of the kidneys, often due to urinary obstruction, a subject to which Dr. Beer has made so many valuable contributions.

The syndrome popularly known as renal rickets was first suggested in 1883 by Lucas (3) who reported a case of albuminuria associated with late rickets. Fletcher (4) in 1911 also noted a relationship between chronic interstitial nephritis occurring in childhood and late rickets, dwarfism and infantilism. However, it was not until 1920 that a clear conception of this disease was established by Barber (5) who introduced the name "renal dwarfism." Since that time numerous case reports have appeared in the literature with a resultant widespread recognition of the disease picture.

In reviewing these reports certain features become apparent. Though the age incidence is variable, the majority of the patients are within the first and second decades of life, the average age being about twelve or just before puberty. Both sexes are equally involved. The most outstanding symptoms are failure to grow, bony deformities, difficulty in walking, increasing weakness, polydipsia, polyuria, and symptoms of uremia. Among the prominent signs are genu valgum, occasionally genu varum, bowing of extremities, frontal bossing, dwarfing and infantilism. The

skin often exhibits a yellow-brown pigmentation, frequently associated with marked dryness and coarseness. Secondary anemia is usual. Thickening of the arteries, enlargement of the heart and occasionally hypertension are present. There is marked impairment of renal function demonstrated by fixation of specific gravity, low phenolsulphonphthalein excretion and severe azotemia. The blood phosphorus is nearly always elevated, while the calcium may be low, normal, or increased.

Several theories concerning the pathogenesis of the condition have been offered. It is almost universally agreed that the kidneys are the primary site of involvement in renal rickets. The majority of cases show evidence of severe chronic interstitial nephritis. Frequently, coexisting congenital abnormalities of the genito-urinary tract are found. These may be in the nature of polycystic kidneys, congenital valve of the urethra, or congenital contracture of the neck of the bladder leading to a secondary hydronephrosis, etc. A few authors favor considering renal involvement as secondary. Chown and Lee (6 & 7) believe that an endocrine dysfunction is the primary factor. They state that a pituitary diencephalic disturbance would explain the malformation of the pituitary gland noted in their case. Such a lesion, too, might explain dwarfing, polyuria, infantilism, and urinary tract dilatation. The nephritis, they postulate, might be due to abnormal mineral metabolism, and the bony changes a sequel of endocrinopathy and not nephritis.

The importance of disturbances in the calcium-phosphorus metabolism in renal rickets is universally accepted. Greenwald (8) first demonstrated that marked impairment of renal function led to phosphatemia due to inadequate excretion of phosphates. Halverson, Mohler and Bergeim (9) discovered low values for serum calcium in nephritis, especially in uremia. The relationship between these two elements tends to be reciprocal. Evidence exists that waste phosphates may be excreted through the intestinal mucosa instead of the kidneys. Mitchell and Guest (10, 11) have suggested that the increased alimentary excretion of phosphorus leads to an increased elimination of ingested calcium by means of the formation of insoluble calcium phosphate. Calcium absorption is thereby markedly diminished, tending to lower the level of the blood calcium.

Albright and Bauer (12, 13) et al. have found secondary hyperparathyroidism a factor in cases where blood calcium and phosphorus changes occur. They believe that hypocalcemia may be a stimulus for parathyroid activity. Smyth and Goldman (14) suggest that hyperphosphatemia, as well as lowered blood calcium, may act as the stimulating agent. Pappenheimer and Wilens (16) report parathyroid hyperplasia in clinical as well as experimental renal impairment. In their post mortem studies nephritics showed a 50 per cent average increase in weight of the parathyroid gland. The severe cases showed an increase of 109 per cent. There seemed to be a correlation between severity and duration of nephritis

and the weight of the gland. Experimentally, Pappenheimer (15) produced extreme renal insufficiency in rats. After a long interval (about five months), the animals were killed and autopsied. Hypertrophy of the parathyroid glands, as well as pathologic changes in the bones, were found. Post mortem examinations have revealed parathyroid hypertrophy in most cases of renal rickets.

Greenwald (17) Hunter (18) et al. have shown that parathyroid hormone causes a marked phosphaturia and mobilization of calcium from the bones into the blood. Aub (19) and his co-workers showed that the initial effect of parathyroid hormone is on the phosphorus. In hyperparathyroidism a lowered renal threshold for phosphorus excretion exists. Albright has suggested that the hormone may decalcify bones directly by increasing the calcium-phosphorus solubility in the serum.

In renal rickets, a physiological attempt at compensation is set up, but is defeated by the initiating cause—that is, impaired renal function. The stimulation of the parathyroid by the hyperphosphatemia could succeed in reestablishing normal phosphorus levels, were the kidneys competent. However, because of the renal insufficiency the only effect of the parathyroid hormone is to mobilize calcium into the blood without affecting the hyperphosphatemia. It is the usual rule then to find an elevated blood phosphorus. The calcium on the other hand can be variable, depending on the balance of the several factors at play—namely, faulty absorption of ingested calcium (excreted as insoluble calcium phosphate), mobilization of calcium from the bones, changes in solubility with varying degrees of acidity, etc.

Severe alterations in the skeletal system are found. Pappenheimer (15) observed that the injection of parathyroid extract in animals suffering from induced renal insufficiency could produce severe osteitis fibrosa. The continued withdrawal of calcium from the bones and the inadequate absorption of the substance lead to marked decalcification and deformity of the bones.

The bone changes have been described radiographically by Parsons (20) as being of three types.

(1) "Atrophic"—appearance like celiac rickets of moderate degree, bones osteoporotic, marked rickets at the epiphyseal line.

(2) "Florid"—shafts seem a little more fragile than the ordinary, appearance like that in infantile rickets.

(3) "Woolly," stippled, honeycomb type—epiphyseal end of the shaft is swollen, forming a large metaphysis. The bone looks moth-eaten as if the shaft were being eaten away subperiosteally. The metaphysis extends over a greater area than in rickets. The skull bones are thickened and show extreme stippling.

Brailsford (21) divides renal rickets into two groups roentgenologically.

(1) The shafts of the bones are of normal shape and density. There

are no osteoporosis, no bowing; the metaphyses are thickened. The diaphyseal ends show cupping with irregularity and fluffiness of their metaphyseal margins. The epiphyseal periphery, however, is well defined, even on its metaphyseal surface. The metaphyseal is disorganized and cannot stand normal stresses and strains, leading to displacement and slipping of the epiphyses. The skull shows no involvement.

(2) This type is usually associated with more severe disturbances. Osteoporosis of the whole skeleton is present. The long bone shafts often consist of coarse cancellous tissue only. There is delayed epiphyseal fusion. The metaphysis is often greatly widened with the diaphyseal end very deep and cup-shaped. The sites of involvement are the same as in the first type but the involvement is greater and the bones show marked deformities with epiphyseal displacement much more frequently. Involvement of the skull is usual. Well defined areas of decalcification in all bones of the skull, associated with a thickening of the parietal and occipital bones are most frequently seen.

Calcific depositions in the subcutaneous tissues and in the walls of the arterial vessels have been described in a few of the cases. Virchow (22) in 1855 first described metastatic calcification occurring in chronic nephritis in five adults. Siegal and Pollack (23) in 1934 described a case of calcinosis in an adult with chronic interstitial nephritis. Karelitz and Kolomoyzeff (24) reported a case in 1932 where calcifications made their appearance after large doses of viosterol had been given. It was believed that this might have been responsible for initiating calcium depositions. To date only three cases of calcification of the arteries in renal dwarfism in children have been reported. In Smyth and Goldman's case five enlarged parathyroid glands were found at necropsy. Platt and Owen (25) reported the case of an 18 year old boy who showed spontaneous calcification. In this case no enlargement of the parathyroid was found post mortem.

The course of the disease is invariably fatal, survival beyond the second decade being unusual. Death usually occurs in uremia. No known treatment is of avail. As pointed out by Smyth and Goldman, parathyroidectomy is valueless. Karelitz has stated that vitamin D and ultraviolet irradiation are ineffectual and perhaps even harmful. Shelling (26) has recommended a low phosphorus diet as most favorable because of the hyperphosphatemia.

CASE REPORT

History (Adm. 405664). A twelve year old female was admitted to The Mount Sinai Hospital March 11, 1937 on the service of Dr. Bela Schick. For the past ten months she had been developing increasing weakness, dyspnea on exertion and difficulty in walking. The child complained of pains in the knees and ankles. It was noted that the child was becoming very knock-kneed. Five months ago the patient was seen

at another clinic where a diagnosis of rickets and anemia was made. The child was given leg braces and received Alpine light treatments; however, her progress continued downhill. During the month prior to admission she was confined to bed because of weakness. One week prior to admission there was a sudden onset of severe sticking pain in the left hypochrondrium.

Past history revealed that during infancy the patient had pyuria associated with fever, lasting several days. At the age of 18 months she was

FIG. 1. March 12, 1937. L. P., age 12 years. The marked genu valgum is evident. Obesity of the trunk and relatively slender extremities are noted. Several pigmented hairy nevi on the face are visible.

said to have an enlarged spleen. She was always obese with relatively slender extremities. Because of excessive weight she had been put on a low caloric diet with resultant loss of seven pounds in the past year. It was observed by the mother that the child had a moderate polydipsia, drinking at least two quarts daily. Polyuria had always been present but never marked. Nocturia occurred twice nightly. There had not been any enuresis. Menses had not as yet begun.

The father died of Hodgkin's disease about one year previously. The mother and maternal aunt both had thyroidectomies for Graves' disease four years ago. There were no siblings.

Examination. The child appeared to have a marked lemon-yellow pallor, somewhat obscured by the dark pigmentation of the skin (partly due to Alpine light therapy).

The trunk was markedly obese with relatively slender extremities. Marked genu valgum was present so that walking was impossible without assistance. The abdomen was very obese and in the left quadrant there was muscle spasm and tenderness. A suggestion of a large mass was believed to be felt on the left side in the region of the kidney. The liver was palpable about 2.5 centimeters below the costal margin. The spleen could not be felt. The heart was rapid in rate, and a soft systolic murmur was audible at the apex. The lungs were clear. Neurological examination revealed no abnormalities. The ocular fundi showed narrowing of the arterial vessels. Blood pressure was 120 systolic and 80 diastolic. The skin was dry and keratotic and had a yellowish pigmentation. Many pigmented and hairy nevi were present, most numerous on the face.

Laboratory data obtained from The Mount Sinai Hospital Out-Patient Department which the child attended nine months before revealed that the urine was of low fixation of specific gravity, albumin ranging from a trace to 3 plus; there was secondary anemia with hemoglobin of 57 per cent. The blood chemistry revealed urea nitrogen of 35 mgm. per cent. Blood pressures varied between 120 to 130 systolic and 86 to 96 diastolic.

Course. The child's course after admission to the hospital was progressively downhill. It was noted shortly after admission that the breath was uriniferous. The blood urea nitrogen at this time was reported as 125, calcium 11.1, phosphorus 6.7, creatinine 5. Urinary function was absolutely impaired; hyposthenuria was present and phenolsulphonphthalein excretion was less than 5 per cent. The blood pressure was 120 systolic and 80 diastolic. Radiographs of the long bones showed marked erosion in the region of the metaphyses, coxa vara deformity of the hips, slipping of the femoral and humeral heads. The skull showed a generalized osteoporosis. The sella turcica appeared normal in size and shape. A roentgenogram of the abdomen revealed definite enlargement of the kidneys and a nodular outline, as in congenital polycystic kidneys. The pain in the left upper portion of the abdomen present on admission, subsided shortly afterwards. She complained frequently of pains in the knees. A low-grade fever appeared and persisted almost daily. Two weeks after admission the heart sounds became distant and tachycardia constant. Pallor and weakness grew more marked. Several transfusions gave only slight temporary improvement in her general condition. One month after admission, an indurated mass suddenly appeared in the coccygeal region, which appeared to be a calcific deposit. This was

confirmed by radiographs. Within the next few days calcific deposits rapidly appeared in the subcutaneous tissues of the buttocks and thighs. Beading of the ribs became prominent. During the next two weeks calcified areas were found both in the upper and lower extremities. The radial arteries became palpably thickened and the peripheral pulses were practically imperceptible. The blood pressure readings were no longer ascertainable. Two months after admission, the right toe became cya-

Fig. 2. Roentgenogram taken April 16, 1937. Widespread calcific deposits are noted in the subcutaneous tissue of abdomen and thighs. Slipping of the femoral head epiphyses and coxa vara deformity are present.

notic, cold, exquisitely tender and painful. The arterial vessels of the fundi which had appeared moderately constricted on admission now appeared much more so.

On admission the girl was placed on a diet low in protein. This appeared to have a slight effect in lowering the blood urea nitrogen. Two months after admission, a high calcium, low phosphorus diet (at the suggestion of Dr. D. Shelling) was started. No appreciable effect on the calcium-phos-

phorus levels in the blood were observed, although the blood urea did diminish somewhat during this time.

On June 29, eleven weeks after admission, the patient was discharged for further care at home. Following this her condition grew rapidly worse. She returned to the hospital one week later in a moribund state and died the following day. Autopsy was not obtainable.

LABORATORY DATA

Roentgenographic Reports. (Dr. M. L. Sussman.) On March 13, 1937 the abdomen revealed enlarged kidneys with nodular outline. Bones, hips,
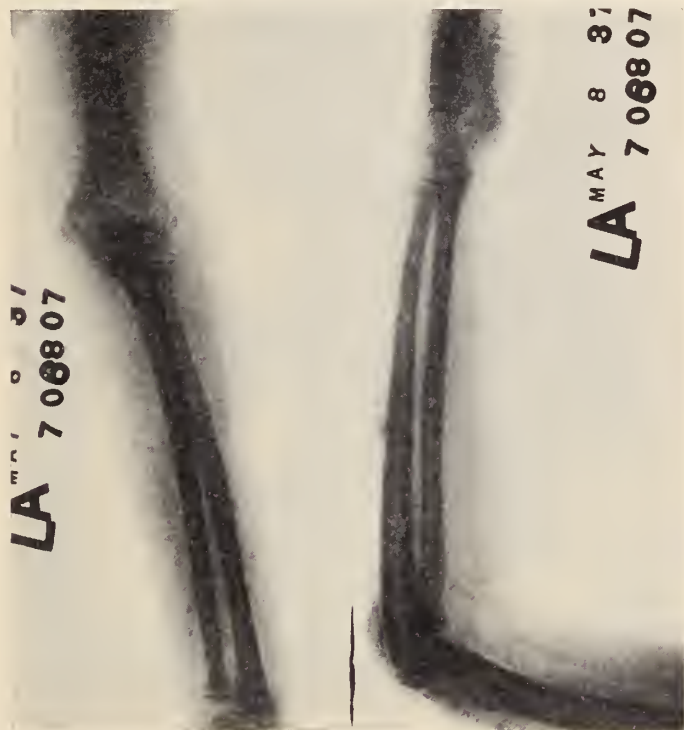
Fig. 3. Roentgenogram taken May 8, 1937. Calcifications in the subcutaneous tissue of the upper extremities and calcified arteries are marked.

knees, and elbows showed marked erosion in the metaphyseal region, associated with coxa vara of hips and partial slipping of the femoral heads. The bones of the skull showed generalized osteoporosis. The sella turcica appeared normal.

On March 16, 1937 the bones of the thoracic cage and shoulder girdles showed marked irregular fraying of the distal ends of the diaphyses. This was also noted in the wrists where marked fraying of the metaphyses of the radii and ulnae was present.

An intravenous pyelogram demonstrated large nodular kidney outlines. The ureters were not visualized because of poor dye concentration.

On April 12, 1937 changes in the vertebrae as in other bones—thickening of the cortices of the vertebral bodies and irregular coarsening of the trabeculae—were reported. Irregular large calcifications about the costochondral junctions were noted on both sides. Irregular calcifications in soft tissues of the buttocks were now seen. Chest showed slight enlargement of the heart to the left with dilatation of the left ventricle. There was noted a soft tissue mass at the root of the neck with displace-

Fig. 4. Roentgenogram taken July 7, 1937. Post mortem perirenal air insufflation clearly defines the nodular outlines of congenital polycystic kidneys.

ment of the trachea. Slipping of the epiphysea of the heads of the humeri was also reported.

On April 16, 1937 diffuse subcutaneous calcification about the pelvis and thighs was noted.

On May 8, 1937 there was marked calcification in subcutaneous tissue and marked calcification of the vessels seen in the extremities on previous examination.

On May 28, 1937 calcifications were noted near both sternoclavicular joints and in the soft tissues about both shoulders. In the neck a soft

tissue mass overlying the jugular notch also showed calcific deposits. The axillary arteries could be seen outlined by calcific deposition.

On June 21, 1937 there was further deposition of calcium in the region of the right upper chest and right lower ribs anteriorly. A marked calcification of humeral vessels was noted.

On June 29, 1937 more calcification of soft tissues about the abdomen and buttocks was reported; also marked calcification of the tibial and femoral vessels.

On July 7, 1937 a post mortem plate showed on perirenal insufflation, bilateral enlarged coarsely nodular kidneys.

Electrocardiograms. On March 12, 1937 sinus tachycardia, right ventricular preponderance, notched P1, high voltage QRS, and inversion of T3 were reported and interpretated as possible enlargement of the right ventricle.

On May 19, 1937 RS-T transitions depressed in lead II and T2 lower amplitude were noted.

Blood Chemistry:

	3/12	3/16	3/23	4/13	5/4	5/22	6/1	6/13	6/21	6/27	7/7
Calcium	11.1	—	11.3	9.8	12.1	10.6	11.7	10.1	10.5	11.0	*2.0
Phosphorus	6.7	—	5.2	4.0	8.5	7.5	6.8	8.0	9.2	8.0	8.0
Phosphatase	—	12 KA units	11 KA units	—	13.5 units	—	—	—.	—	—	12 KA units
Urea	125	—	145	110	91	81	49	88	120	100	178
Creatinine	5	—	—	5	7.5	—	—	—	—	—	16
Chlorides	—	470	—	490	555	580	665	—	—	—	365
CO_2	—	43	—	—	—	—	—	—	—	—	38
Cholesterol	—	—	—	—	—	340	—	—	340	305	370
Sugar (Janney)	100†	—	—	—	—	80	—	105	—	—	—
Total protein	7.7	—	—	7.5	6.1	6.1	—	—	7.0	—	7.1
Albumin	5.2	—	—	4.6	3.0	4.2	—	—	—	—	5.3
Globulin	2.5	—	—	2.9	3.1	1.9	—	—	—	—	1.8

* Taken one hour after death.

† High prolonged.

Urine Analyses. March 12—Fixation of specific gravity 1008–1010. Phenolsulphonphthalein excretion test—less than 5 per cent. March 12–July 7—Albumin ranged from a trace to 2 plus. Sugar and acetone negative. Microscopic examination—occasional white blood cell per high powered field. From May 22 on, many white blood cells, occasional red blood cells, and granular casts were present. June 27—Catheterized urine for culture reported negative. July 7—Catheterized urine for residual reported negative.

Blood Counts. March 12–July 7—Severe secondary anemia: Hemoglobin ranged between 38 and 32 per cent; average red blood cell count, 2.5 million; average white cell count, 9500; average differential count normal.

Basal Metabolism. March 12—1147 calories (Normal 1260 calories). May 4—1176 calories.

Hormone Excretion Test. March 16—normal.

Hamilton Test for Parathyroid function. April 13—questionably positive for hyperfunction. April 24—negative for hyperfunction.

Visual Field Examination. March 16—normal.

COMMENTS

In our case the fundamental lesion was unquestionably in the kidneys. These were congenitally polycystic, as demonstrated by ante and post mortem radiographs. The value of perirenal air insufflation in demonstrating the kidney outlines was emphasized here. It is a procedure to be borne in mind, particularly in cases where the renal concentrating function is so poor as to render intravenous pyelography unsatisfactory. Infection was undoubtedly superimposed upon the congenital abnormality. In this regard the episode of pyuria in infancy was significant. This added burden on already defective kidneys was sufficient to bring about an absolute impairment of renal function.

A very interesting feature was the sudden spontaneous appearance of calcifications in the subcutaneous tissues and in the walls of the arteries. The dry gangrene of the toe was brought about in this manner by the extreme arterial sclerosis. It is noteworthy that at the time these depositions took place the serum calcium and phosphorus values fell to normal levels only to rise again when new depositions ceased appearing.

Unlike Karelitz's case where vitamin D in the form of large doses of viosterol was given and incriminated as a cause for the calcifications, we could not determine the initiating factor here, since calcification appeared in the soft tissues and vessels in the absence of antirachitic therapy. It is of interest that while our patient was on a low phosphorus diet, the calcium and phosphorus levels in the blood serum appeared unaffected. The blood urea, however, did drop to a lower level and the patient appeared brighter and more comfortable.

The bony deformities in this patient were of the usual variety. Genu valgum was most prominent. Judging from the severity of the metabolic disturbances, it is surprising that radiographs of the bones did not show much osteoporosis. The roentgenological findings fell rather into the first group in Brailsford's classification in which the roentgen pathology seems to be confined to the metaphyses of the long bones.

In our case there were definite indications of a pluriglandular disturbance. An hereditary factor was suggested by the family history of hyperthyroidism. Endocrine stigmata in the patient were several— the obesity (of the pituitary type), the high prolonged Janney curve, the low basal metabolism, the dark pigmentation of the skin and multiple hairy nevi.

Unfortunately no autopsy was obtainable so that the state of the parathyroid glands could not be determined. The Hamilton test for hyperparathyroidism was performed on two occasions, once being suggestively positive, the second time negative. The phosphatase and ionized calcium values in the blood serum were within normal limits which also did not favor hyperfunction of the parathyroid.

It is not unlikely that the thyroid, pituitary and other endocrine glands are involved in renal rickets. As stated above, Chown and Lee reported a case in which a pituitary lesion was found in necropsy. Siegel and Pollack's case had hyperthyroidism. The thyroid and pituitary glands apparently play some rôle in calcium-phosphorus metabolism. Aub and Bauer (27) have shown that thyroid extract causes increased excretion of both substances. Indeed bone decalcification has been noted frequently in hyperthyroidism. On the other hand, hypofunction of the thyroid is associated with diminished excretion of calcium and phosphorus. Adrenalin, insulin and pituitrin (28) have been found to cause transitory increases in the serum calcium. Pappenheimer (15) has also observed that the injection of anterior pituitary extract caused hypertrophy of the parathyroids in rats and rabbits. We are faced then with a complex maze of inter-relationships among the endocrine glands which can apparently influence and be influenced by the blood calcium and phosphorus.

From a survey of the literature and a consideration of the facts now known concerning renal rickets, the theory of its pathogenesis as elaborated and recapitulated by Park and Eliot seems most plausible. The original damage is in the urinary tract; either a congenital or an acquired impairment of the kidney exists. Salts cannot be excreted and phosphorus is retained in the blood in excess of the normal amount. The hyperphosphatemia acts as a stimulus to the parathyroid gland which, in turn, affects the metabolism of calcium and causes changes in the bony skeleton. Park and Eliot, moreover, have shown that the bone changes are not strictly characteristic of rickets and have therefore proposed the name renal hyperparathyroidism in place of renal rickets. In spite of the validity of this conception, the term renal rickets has become so fixed in the literature that we have seen fit to describe our case under this title.

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ACUTE PANCREATITIS

A Review and a Report of Ten Verified Cases

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As far back as 1856 Claude Bernard, working on ferments and digestion, produced hemorrhagic pancreatitis in animals by injecting into the pancreatic duct a mixture of bile and oil. The interest in this causal relationship was intensified when, in 1901, Opie described his case of acute pancreatitis associated with a gall stone impacted in the papilla of Vater and reported that he had produced an essentially similar pathological process by injecting bile into the pancreatic duct. Since that time there has developed a voluminous literature on this subject and the various chemical and physiological elements which it comprises. Yet, in all the extensive reports of the innumerable experiments purposed to establish the pathological physiology, the chemical processes and the relationship of mechanism of production to variation in anatomic structures, there is a striking paucity of contributions to treatment. Behind this mass of experimental work there seems to be the implied conviction that the etiological factors must be established as the first steps in developing methods of prevention, and that surgical treatment seems to have reached a stage that offers little prospect of immediate further aid in the treatment of this condition whose mortality averages 50 to 60 per cent—a figure practically unchanged for about thirty years.

Acute pancreatitis, while infrequent in the experience of any one man, yet totals a huge number of cases. It involves an organ which is peculiarly situated in the abdomen, retroperitoneally, is in close contact with the celiac plexus, is richly supplied with lymphatics and has manifold functions. These facts, coupled with the difficulty in diagnosis, the varied and unexplained pathology, the contradicting and unaccepted causes, and the very serious prognosis, offer complexities that challenge attention and study.

ETIOLOGY

Some sort of an etiological outline must be used in any attempt at an orderly presentation of the subject. A modification of McWhorter's table seems most satisfactory (Table 1). However, no table may show sharp distinctions in classification because they are not to be found, as there are too many interacting and coexisting factors.

In the classification of the non-infectious causes, the mechanical status which permits the entrance of bile into the pancreatic ducts is by far the most important, as it apparently accounts for a large majority of cases. The occurrence of this "biliary reflux" depends largely on the anatomic arrangement of the common bile duct and the pancreatic duct at the papilla of Vater. Opie's "common channel" theory presupposes that,

TABLE 1

Etiology of Acute Pancreatitis

A. *Non-infectious Origin*
  1. Mechanical formation of a "continuous channel" with resulting biliary reflux. Due to:
    a. Obstruction of papilla.
    b. Spasm of sphincter Oddi.
  Followed by:
  2. Chemical action on pancreatic cells by:
    a. Bile; or, in other instances, hydrochloric acid, etc. in regurgitated duodenal contents.
    b. Activated trypsin.
  3. Injury to pancreatic tissue. (This may or may not be followed by infection.)
    a. Vascular accidents: thrombosis, embolism with infarction, hemorrhage on arteriosclerotic basis.
    b. Hemorrhage in benign or malignant growths.
    c. Trauma: gross: causing massive tissue destruction.
             operative: causing edema of papilla or reflex spasm of sphincter Oddi.
B. *Infectious Origin*
  1. Via the lymphatics, particularly from the duodenum and gall bladder.
  2. By direct extension from infection in any adjacent structure.
  3. Infected bile or duodenal contents entering a pancreatic duct. This effect is generally associated with A:2
  4. Hematogenous infection, as part of a continued or transient bacteremia, involving normal pancreatic tissue.
  5. Infection of damaged, necrotic or neoplastic tissue via the blood stream, or by organisms found in the normal gland.
C. A combination of conditions from A and B.
D. Idiopathic cases.
  Mechanism unrelated to A:1
  Relationship to other body states not understood: pregnancy, acute yellow atrophy of liver, diverticulum of duodenum, etc.

because they usually join a short distance above the exit into the duodenum, these ducts are converted into a continuous channel when the papilla is obstructed. He and others state that this common channel can be created in 70 to 80 per cent of bodies. Mann and Giordano, however, working with fixed specimens, report that only 5 per cent of them show the ducts in an arrangement that would permit this. Cameron and Noble criticize this work with fixed tissues and state that by carefully

obstructing the papilla with a gall stone and then making casts of the distended ducts, they find that a common channel is created in 65 per cent of cadavers. These results were obtained in work on "normal" specimens. What these figures are in actual cases of pancreatitis it is impossible to say, as no data on the subject are available.

While this theory of a common channel formation offers a ready explanation in those instances in which the papilla is obstructed by an impacted gall stone, it happens that such a stone, popularly thought to be of common occurrence, is actually found only in about 5 per cent of cases of acute pancreatitis. Therefore, a spasm of the sphincter of Oddi has been suggested as another probable cause for the common duct obstruction, and is considered to be a functional disturbance, similar to pylorospasm, occurring in biliary tract disease. Such a spasm has been produced by the introduction into the duodenum of a 3 per cent solution of hydrochloric acid. It is to this spasm that are ascribed the instances of acute pancreatitis following cholecystectomy with instrumentation of the duct. This is presumed to be the result of direct irritation of the sphincter or the effect of manipulation of the nerve structures in that region.

The differential pressure between the bile ducts and the pancreatic ducts is supposed by itself to play little part in the production of the biliary reflux, even though the pressure in the bile ducts is known to be considerably higher than in the ducts of the pancreas, particularly at the height of digestion. The reflux into the pancreatic duct is made possible, once the duodenal exit is obstructed, by the fact that a reduction in the intra-pancreatic duct pressure can occur because of the anastomosis between the branches of the ducts of Wirsung and those of Santorini. Opie, Baldwin and others have shown that this anastomosis is very extensive in 70 per cent of specimens. This anastomosis permits a reverse flow of pancreatic juice as the bile enters the pancreatic duct and, therefore, a release in pressure in the branches of the duct of Wirsung into those of the duct of Santorini and out through its opening, if patent, into the duodenum. The flow of bile into the pancreatic duct might be further aided by the increased pressure in the common duct due to gall bladder contractions during the height of digestion. Robins showed that this reverse flow does occur in presenting the case of a patient who died of acute pancreatitis, without operation. The autopsy showed a large number of small stones in the hepatic ducts, gall bladder, common duct, papilla of Vater and also in the pancreatic duct and its radicles (fig. 1).

That interchange of contents between the bile and pancreatic ducts may be influenced by their differential pressure is shown by some observations made after a cholecystostomy or choledochostomy, when the pressure in the biliary tract is considerably lessened. Large amounts of pancreatic juice were recovered in the biliary drainage. Shönbauer also reports finding trypsin in the sterile bile in a case of acute cholecystitis.

For a similar reason, after cholecystectomy, increased bile duct pressure with reflux into the pancreas has been reported to have caused acute pancreatitis before the normal adaptations after such an operation have taken place, namely, the dilatation of the bile ducts or the development of incontinence of the sphincter.

Obviously, the common channel theory can have no place in the causation of acute pancreatitis when the pancreatic and bile ducts enter the
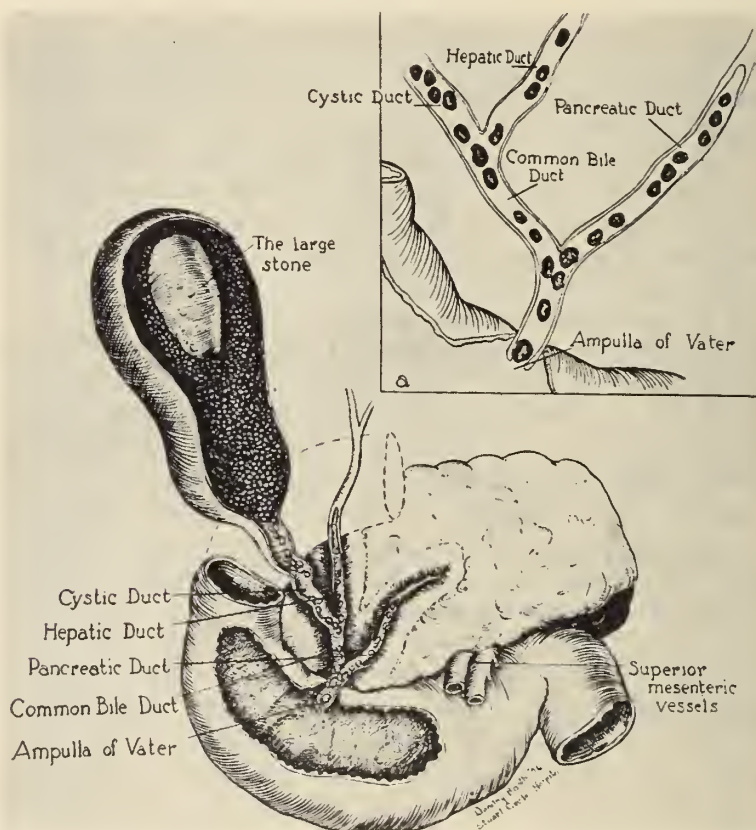
FIG. 1. Drawing from specimen. Stones in the pancreatic duct are similar in every way to those in the gall bladder, and were composed of cholesterol (Robbins).

duodenum separately, as is the case, according to Baldwin, in about 20 per cent of individuals. This is particularly pertinent when the pancreatic lesion is found limited to the tissue drained by the accessory duct which has no sphincter to protect its orifice. In these instances it is believed that the regurgitation into the duct of duodenal contents containing hydrochloric acid, or bile, or bacteria, may cause the pancreatitis. Polya obtained this result in experiments which reproduced the regurgitation.

The source of the increased intra-duodenal pressure required to force the duodenal contents into the pancreatic duct is yet to be discovered. Severe vomiting, with its increased intra-abdominal pressure, has been accepted as an occasional factor, but it is too infrequently associated with acute pancreatitis as cause and effect to receive serious consideration. Furthermore, large neoplastic deposits have caused mechanical conditions in the duodenum resulting in increased intra-duodenal pressure and permitting the free flow of duodenal contents into the pancreatic duct without a demonstrable reaction in the pancreatic tissue. It has also been shown that Wirsung's duct may become filled with the media used in X-ray studies to outline the gall bladder and common bile duct (Gatewood). This would indicate duodenal regurgitation without clinical results.

An incidence of about 60 per cent of biliary tract disease is reported to be associated with acute pancreatitis. If the relationship of infection is excluded, then direct proof of a mechanical element in the causation can be shown in only 5 per cent of cases, i.e., the instances with an impacted gall stone. Many patients, moreover, are found to have a gall stone impacted in the papilla (some for long periods) without the development of acute pancreatitis. Does the hypothetical spasm of the sphincter of Oddi account for all those other cases in which a biliary reflux apparently occurs? Is some other pathological physiological process responsible? These are merely two questions on the existent uncertain etiology of the condition. Other causes given for obstruction of the papilla are a round worm, an inflammatory swelling and an edema of the duodenal mucosa around the papilla due to venous stasis. Baló and Ballon report three such cases of acute pancreatitis in which the edema was present because of cardiac decompensation.

THE MECHANISM OF BILE PANCREATITIS

The entrance of bile into the pancreatic duct initiates a series of chemical reactions. Flexner has shown that the taurocholates are the bile ingredients mostly responsible for the effect on the pancreas. Brocq and Binet found that only sodium glycocholate was particularly effective in this respect. Archibald, in his work, used a solution of the sodium salt of either acid in a concentration equal to that in the bile. He and others have demonstrated that infected bile has a higher salt content than normal and is, therefore, more potent in its action. Gall bladder bile, too, is known to be more concentrated than that in the ducts.

It has been found that normal pancreatic tissue possesses the same immunity to action upon it by trypsin which the stomach epithelium has to that of the gastric juice. In fact, it seems proved that the pure enzymes trypsin and pepsin, as such, cannot attack any living tissue, but are dependent on the alkali or acid in the respective juices to initiate the process of digestion which they then help to maintain. Dragstedt demon-

strated, in an interesting series of experiments, the resistance of uninjured pancreatic tissue to all attempts at digestion. He called attention to the frequency with which the pancreas forming the floor of a large chronic perforating gastric or duodenal ulcer is found to be normal in spite of the long exposure to the digestive process.

The bile salts have a necrotizing effect on the pancreatic cells, duct and acinar, which seem more susceptible than those of other tissues, particularly when in the secreting state. The immediate effect of the contact of cells with bile salts is an outpouring of blood or only blood serum—a protective reaction, since the large colloidal protein molecules combine with the bile salts and so lessen their diffusability and inhibit their action. Perhaps the bile also activates the trypsin. This activation is certainly furthered, if not initiated, by the products of cytolysis and, according to Finney (though other opinion is against it), by the calcium of the extravasated blood serum. The trypsin shortly destroys the protein molecule holding the bile salts, setting them free to produce further cell damage. The introduction of bile into the pancreatic duct causes an almost immediate reaction, so that the edema and hemorrhage mentioned may become extensive and severe in a very short time. When the process stops at this stage there may be complete restitution of the involved tissue, but when it is more severe there results a diffuse or local necrosis of the parenchyma. Perhaps this rather common assumption that the edema, hemorrhage and necrosis represent gradations of a single process is erroneous. Perhaps the development of the last, as some believe, has another basis. There is, however, no proof of this.

It is this necrosis and its sequellae which cause the toxemia and shock so often fatal in acute pancreatitis. The symptoms are due to the absorption of one or more proteolytic substances, probably a histamine, produced in the necrotic tissue or peritoneal fluid by bacterial action. The most common of these bacteria is B. coli, but the most important one is similar to, if not identical with, B. welchii. They are thought to enter the pancreatic ducts from the duodenum and remain inactive. The presence of B. welchii in the peritoneal fluid may be due to its passage through the intestinal wall because of peritoneal irritation.

Dragstedt's work on this subject of toxemia and shock has clarified some uncertainties and eradicated misinformation which has been allowed to stand for years. He showed definitely that the intraperitoneal injection of active pancreatic juice or the products of pancreatic digestion or autolysis, if sterile, was practically non-toxic. Similarly, the peritoneal implantation of sterile pancreatic tissue with subsequent autolysis caused no symptoms. The use of non-sterile material, permitting the access of bacteria or the growth of those already present in the pancreatic tissue, caused the characteristic group of symptoms to develop. This work disproved any non-specific proteid theory, or the effect of pan-

creatic secretion or extract in producing the toxemia. Other workers, including Whipple and Cook, have given to animals intraperitoneal

FIG. 2. Secondary infection of the head of the pancreas following an injection of the ileo-cecal ganglions (Braithworth).

and intravenous injections of peritoneal fluid (apparently not infected) from cases of acute pancreatitis without toxic effect.

Much doubt has been thrown on the importance of a vaso-depressor reported by Goodpasture as present in normal fresh pancreas. Judging by the amount of pancreas needed to provide a fatal dose, even when given intravenously, it seems to be present in quantities too small to be of importance clinically, especially when the slow rate of absorption from the peritoneal cavity is considered.

In discussing the infectious causes of acute pancreatitis, that resulting from lymphatic spread should be mentioned first. The lymphatics of the pancreas (figs. 2 and 3) have been shown to anastomose freely with
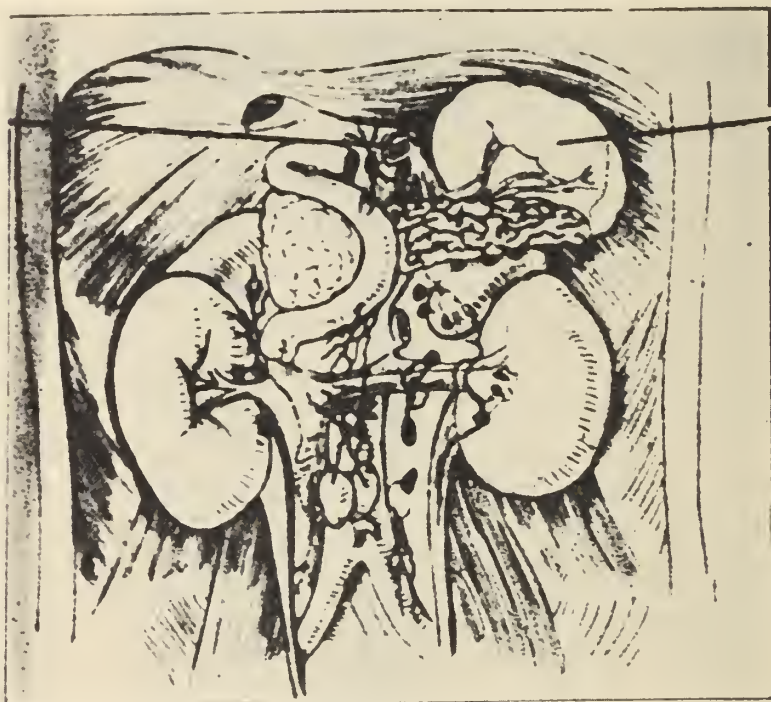
Fig. 3. Relations of the lymphatic vessels of the pancreas. *c.* cardia; *sp.* spleen. (After Bartels).

those of the liver, gall bladder, duodenum, and caecum and appendix, particularly with the first three. The likelihood of the lymphatic spread of infection from these structures to the pancreas is not fully accepted. Those favoring it cite the subacute and chronic pancreatic changes affecting especially the interstitial tissue found in about 30 per cent of cases of chronic gall bladder disease. This points to the possibility of this path of infection for chronic processes and raises the question whether it may not serve similarly as a route in the acute cases. Deaver, Judd, Graham and Peterman have written extensively favoring this belief. Experimental

evidence for the lymphatic extension is not abundant, but surgeons believe in its probability because there is too much clinical evidence to be disregarded. Others, however, call attention to the large number of unoperated cases of acute cholecystitis without pancreatic involvement. They also say that the type of lesion found in the pancreatic tissue differs from the one at the original site of infection and that the abscesses which are found early in the disease and the residua seen when the acute phase has subsided are unusual in infectious processes. Similarly, objections are raised to cases reported by competent observers as showing the pancreas involved by direct extension from an infectious process in some adjacent structure, most often a duodenal ulcer.

Single or multiple hematogenous pancreatic abscesses need no special emphasis. They occur as a rule in a gland previously normal. The secondary infection of tissue that is damaged or necrotic as a result of acute pancreatitis is another matter. Here, while the invading organism may be blood borne, it is often an aerogenous anaerobe, probably B. welchii, found indigenous to the pancreas of every laboratory animal and presumably also of human beings.

When all the more or less accepted causes of acute pancreatitis have been duly accredited, there are still left about 25 per cent of cases for which no explanation is known at present. These are the so-called "Idiopathic" —a group which one hopes will steadily diminish. Under such a heading must be placed two of the cases reported here as associated with acute yellow atrophy and a normal pregnancy.

SYMPTOMS

Acute pancreatitis in childhood presents a clinical picture very similar to that seen in adults, but is rarely recognized because it is seldom suspected. Dobbs reports fourteen cases, only one of them his own. In six instances the etiology was entirely unknown. Among the others were some associated with mumps, others after tonsillitis, etc.—indicating a probable hematogenous route of the infection. Three were caused by obstruction of the papilla by an ascaris, and one was initiated by a stone impacted in the ampulla. Of the others, several were due to direct trauma. In all the cases the pancreatic processes were apparently severe and not merely an edema, as some observers think is the condition usually found in children.

In adults, the symptoms of the onset vary considerably depending upon the condition with which the pancreatitis is associated (gall bladder disease, vascular injury, etc.). This explains why so many cases are undiagnosed until operation, or, if they are mild attacks, remain unsuspected in the patient's history, to be recognized by the residua seen in a subsequent laparotomy. In the fulminating attack the picture may be confused with one due to perforated gastric or duodenal ulcer, or intestinal obstruction.

Pain. In the acute attack the outstanding symptom is the sudden onset of a sharp and boring pain. It may be mild or very severe, constant or intermittent, and may be localized to the epigastrium or radiate widely. Often the radiation is to the right upper quadrant, at times to the left, or straight through to the left flank, the last being a rather characteristic site.

Tenderness is conspicuously absent at first, regardless of the severity of the pain. Similarly, there is no abdominal rigidity at this stage. However, as the pancreatic involvement becomes definite and the peritoneal irritation sets in, tenderness and rigidity become marked and are localized to the epigastrium. In a comparatively short time, however, they may become very diffuse. Tenderness appearing in the left costo-vertebral region is of diagnostic significance. Edema may appear and cover a considerable area. The occasional almost total limitation of the tenderness and radiation of pain to the right upper or lower quadrant creates a confusing element in diagnosis.

Vomiting begins early and may become severe and protracted. At first it is the nondescript symptom of an intra-abdominal pathological condition, but later it becomes part of a toxemia or even an ileus. It may cause severe loss of water and salt.

Prostration. Within a few hours or a day or two characteristic prostration sets in, which rapidly changes to shock or collapse with its usual picture of an abrupt fall in blood pressure, rapid thready pulse, and pale, cold, moist skin. It may be associated with continuous vomiting, the vomitus gradually becoming blood tinged.

Due to diaphragmatic irritation, severe and uncontrollable retching and hiccough appear and add greatly to the patient's misery. *Obstipation* may develop with marked abdominal distention, or even a toxic paralytic ileus.

Jaundice is seen occasionally as the result of liver cell degeneration, but it may be due to common duct obstruction by an inflammatory reaction in the head of the pancreas. A toxic jaundice almost always foretells a fatal outcome.

Fever. Rise in temperature is inconstant, and its variations are not indicative of conditions either in the pancreas or the peritoneal cavity.

Hemorrhage. Blood coming through the pancreatic duct occasionally appears in the stools; it is usually small in amount. The bleeding, however, may be so profuse that, when considered with the rest of the clinical picture of pain, vomiting and shock, it suggests a mesenteric thrombosis. The severe bleeding is due, at times, to a necrotizing duodenitis or gastritis. The bleeding from either source may show itself also as a hematemesis.

Blood Findings. A white cell count, total and differential, as well as the percentage of polymorphonuclear neutrophiles with toxic granules, are of little diagnostic or prognostic value.

Glycosuria may occur at the outset and has no significance in the diagnosis or prognosis. It varies considerably in degree and usually clears up in patients going on to recovery, whereas it becomes more severe and accompanies as an increasing hyperglycemia in the fatal cases. A normal urine does not always mean a mild case. This subject is considered in detail further on.

Epigastric Mass. In patients who have survived the acute phase there may be noted the gradual development of a smooth, tender epigastric mass, variable in size. This may be the enlarged, hemorrhagic pancreas, a thickened, rolled up omentum, a pseudo-cyst or localized abscess, or a localized retroperitoneal hemorrhage. This mass, whatever its nature, is found at times within a few days after the onset of the attack, but generally, as indicated above, appears only in two or three weeks. Occasionally it is not detected until months after the attack when the time of its development cannot be accurately determined.

Rochet stresses the need for the recognition of the milder, subclinical forms of acute pancreatitis which are represented by the indefinite picture of prolonged epigastric pain and distress, vomiting, and with or without a rise in temperature, etc. The true nature of these conditions should be recognized and the patient studied with the object of preventing acute attacks. The results of these milder attacks are frequently seen at subsequent operation as the peritoneal scars of fat necrosis, areas of pancreatic induration, etc., often associated with gall bladder disease.

PREDISPOSING CAUSES

Adiposity and alcoholism have definitely been shown to be important causes predisposing to acute pancreatitis. Ten per cent of attacks are reported to occur in severe alcoholics.

In a group of sixty-five cases reported by McWhorter, over 50 per cent gave a history of acute or chronic gall bladder disease, and about half of these had an acute infection. Over half of the total number gave a history of attacks of upper abdominal pain and distress which, in view of subsequent developments, must be interpreted as due to mild pancreatitis. Beckman also stresses the great frequency of premonitory attacks and quotes Körte who found that they are frequent even in patients who have no gall bladder disease but subsequently develop acute pancreatitis.

COMPLICATIONS

Parotitis is rare, and may occur *after* the onset of the pancreatitis. Interestingly enough, the association with parotitis, as mumps, is seen more frequently in young adults than in children.

As a result of pancreatic suppuration a local thrombophlebitis may occur, with a consequent bacteremia of varying duration. Not infrequently the splenic vein becomes thrombosed for the same reason, with

splenomegaly as a result, if the duration of life is sufficiently long. Serious kidney damage may be caused by the excretion of trypsin when it enters the blood in large amounts (Beckman) and hematuria, albuminuria, varying degrees of azotemia, and even a fatal anuria may follow.

The development of a paralytic ileus is rather common, with the attendant loss of water and inorganic salts through vomiting, resulting in dehydration, diminished blood chlorides and varying degrees of alkalosis. The increase in non-protein and urea nitrogen described with intestinal obstruction is present here, too. Postoperative wound digestion is unusual.

PROGNOSIS

At best the prognosis is very bad, since forty-five to sixty per cent of the patients die. The outlook is worse in the obese and in the alcoholic. Women who have had multiple pregnancies apparently stand the condition as well as others. The mortality is not higher in young people than in old, but is decidedly so in the gangrenous type of the disease and with extensive involvement, even if the process is only hemorrhagic. The prognosis in lesions of the head of the gland is emphasized as bad. However, recovery may take place despite the occurrence of surprisingly large sloughs of the pancreas.

DIFFERENTIAL DIAGNOSIS

It is apparent that in the majority of cases in which the condition was missed, it was because the diagnosis was not considered. Fitz, in 1889, wrote: "Acute pancreatitis is to be suspected when a previously healthy person or a sufferer from occasional attacks of indigestion is suddenly seized with violent pain in the epigastrium, followed by vomiting and collapse and, in the course of twenty-four hours, by a circumscribed epigastric swelling, tympanitic or resistant, with a slight rise in temperature." Clinicians agree that a careful history is of great help. The diagnosis, by direct evidence or by inference, of a previous gall bladder attack, mild or severe, should suggest the possibility of pancreatic involvement in the presence of an acute abdomen. It should be remembered that while gall bladder disease and gall stones are about 50 per cent more common in women, the occurrence of pancreatic necrosis is almost that much more frequent in men.

In the differential diagnosis one must consider the following: gastric crises of tabes; perforated gastric or duodenal ulcer, in which the history of previous pain after meals or while fasting and the relief by medication, is significant. In the perforated ulcer the peritoneal irritation occurs at once and spreads very rapidly so that abdominal rigidity becomes diffuse in a very short time. In acute pancreatitis the abdomen is known to be soft for the first few hours, or the rigidity, if present, is limited to the epigastrium. The demonstration of free air in the abdomen is diagnostic

of perforated ulcer. The radiation and localization of pain in acute appendicitis and acute pancreatitis occasionally is in the same area. In the former condition the story of the localization of the pain for some hours without change is an important fact, and the shock which is characteristic of the latter condition will occur only with rupture and a developing peritonitis. Intestinal volvulus, or obstruction due to another cause, will rarely have the severe epigastric pain, the extreme tenderness over the pancreas or in the left lumbar region, which is seen so frequently in pancreatitis. In this one instance the total white cell count may be an important diagnostic aid because in the early hours of intestinal obstruction it is rarely elevated to any extent. An X-ray plate of the abdomen will frequently indicate the diagnosis of obstruction by showing loops of distended gut with fluid levels. Mesenteric thrombosis may offer some difficulty, especially in older people in whom arteriosclerosis could account for either condition. Acute gall bladder disease offers a considerable diagnostic problem, particularly if the roentgenogram does not show stones. In these cases the delay of a few hours is relatively unimportant; yet in this period the characteristic picture of a pancreatitis will have become established to some extent. A coronary thrombosis, with atypical epigastric radiation and continuous pain, may create some confusion. The rapid drop in blood pressure with the early appearance of shock may add to it. Here, the previous history and a few hours of observation may disclose the real cause.

LABORATORY AIDS IN DIAGNOSIS

Tests for Ferments. In instances of pancreatic destruction, methods for the detection and quantitative determination of pancreatic ferments liberated into the blood have received considerable study. Wohlgemuth's test for amylase is used widely—100 c.c. of blood will normally contain enough amylase to produce up to 200 mg. of sugar in the reagent. In acute pancreatitis this figure may reach two or three thousand. It is a mistake to do this test once or twice only; to be of value it should be repeated several times so that comparative figures for a longer period may be obtained, inasmuch as the early figures may approach normal limits. Repeated tests also give some indication of the progress of the disease. Elman and others state that the amylase findings and the clinical pictures seem to indicate a definite relationship between the quantity of amylase in the blood and the condition of the pancreas. Böse, after performing a large series of tests, reported that the figures may return to normal within a few days if the pancreatic involvement is mild. From the point of view of diagnosis, continued normal readings furnish strong evidence against pancreatic destruction. A change toward normal may be very abrupt after cholecystostomy and relief of pancreatic back pressure. Where there is progressive pancreatic necrosis, however,

a similar subsidence of a high amylase figure may take place, but the reason for this is naturally obvious. Then, too, the clinical picture is one that displays a steadily downward course, in contrast to the cases in which the drop in the figures is associated with an improvement that goes on to cure. The evidence at hand suggests that the main source of the blood amylase is the pancreas. Instances in which no pancreatic disease is found and in which there has, nevertheless, been a high transient amylase content in the blood may be due to the temporary obstruction of the main pancreatic duct.

The test for lipase is relatively new and, though considered in European clinics to be very valuable, does not meet with much approval in this country and is thought by many workers to be worthless. However, Comfort, of the Mayo Clinic, reports an increase in blood lipase in seventeen out of twenty cases which clinically suggested acute pancreatitis and at operation showed pancreatic disease to be present. Böse maintains that the lipase seems to be released and to appear in the blood as soon as the process in the pancreas begins. Some believe it to be a delicate test and of greater value in chronic pancreatic disease.

The determination of urinary diastase as a test is only moderately popular. Generally it is found to be elevated in pancreatic destruction. The normal urinary content (up to thirty units) may rise to two hundred, five hundred or even a thousand. This test lacks recognition because it is not specific. It may be found strongly positive in diabetes and other conditions. However, it may be of assistance when taken in conjunction with a clinical picture suggesting pancreatitis, because the figures are so outstandingly high. Böse does not consider this test to be of much value.

Glycosuria may be present and vary greatly in its severity. Coupled, of course, with hyperglycemia, its onset in the later stages of acute pancreatitis is important as an indication of failure of pancreatic function. A rapid continued rise in blood sugar and sugar excretion may be of value as a gauge of progressing pancreatic destruction. Nevertheless, observers comment on the high grade of hyperglycemia and glycosuria which appear to be compatible with recovery when the remaining pancreatic tissue regains its full functioning power. After recovery, glucose tolerance tests usually show normal results. This conforms with the common knowledge regarding the huge factor of safety possessed by the pancreas. During the acute and early recovery stages modified sugar tolerance tests have been done using only 50 grams of glucose. The blood sugar curve presented is of interest, inasmuch as a maximum figure is reached in about forty-five minutes, a period considerably shorter than that seen in diabetes, in which the rise is more gradual.

A hypercholesterinemia has frequently been reported, and may become sufficiently high to cause a milky serum.

In what is grossly called acute pancreatitis the pathological state of the pancreas may vary considerably. The well known intense edema, hemorrhage, and localized necrosis are considered by most observers to be gradations of the same process and to vary according to the intensity of the causative factor. It is the necrosis, especially when extensive, which really constitutes this disease. The milder reactions may clear up, leaving no evidence, or they may produce the induration and fibrosis mentioned previously. Some observers believe that these conditions are the results of different mechanisms, in other words, not a matter of degree, but of type.

The amount of glandular tissue affected may vary from a small area about a main duct or one of its larger radicles to a total or subtotal involvement of the gland. The areas of slough may vary in size and number and may occur in hemorrhagic or bile stained tissue. There is the frequent finding of a single area of tense edematous tissue usually near the head of the pancreas, but rarely is the entire gland similarly affected. In patients whose histories suggest that there have been previous mild attacks of acute pancreatitis and who are operated upon during a severe recurrence, there may be found areas of dense fibrosis which replaced previously destroyed or atrophied portions. This fibrosis may be present in some degree throughout the entire gland indicating the wide extent of the previous inflammation. A single fibrotic area, if small and dense, has frequently been mistaken for neoplastic tissue, its true character being disclosed on microscopic examination. Occasionally some of these fibrosed areas show on section a thick cheesy material which represents inspissated necrotic tissue. On culture this material is sterile. Frank pus is rarely found. Calcification has been described which at times is dense enough to show on a roentgenogram.

Pancreatic cysts with contents varying in the admixture of blood, fluid, and sterile necrotic material are known to develop after an attack of acute pancreatitis. Some of these are pseudocysts inasmuch as their histological formation and contents exclude them from the classification of true cysts. They may appear early or late and have been found in the pancreatic area from a few hours to weeks or months afterward. Occasionally they are not found until two or three years later, but these observations are open to question because the patients were not examined at short intervals.

Rich and Duff report that in the pancreas of twelve out of twenty-four individuals affected by acute pancreatitis a metaplasia of the duct epithelium was present, which caused obstruction. It was irregular in distribution and resulted in partial or complete obliteration of the lumen. In their opinion the subsequent distention and rupture of the smaller ducts

and acini produce a hemorrhagic pancreatitis with all the sequellae. The cause of acute pancreatitis is, therefore, considered to be intrapancreatic and not external. If this observation is correct, surgical attack could hardly find the involved areas or bring about any beneficial changes. This mechanism does not explain how any case may clear up spontaneously, or, if it does, how it can remain so without recurrences.

Fat necrosis is present in 75 to 80 per cent of cases of acute pancreatic disease, but is less frequently seen in the extensively necrotic or suppurative lesions. While bile is generally accepted as playing the major part in the production of this fat necrosis, the rarity of its occurrence in sudden extensive pancreatic destruction is explained in the neutralization of the lipase by the products of autolysis. The fat necrosis may be localized to the region around the pancreas or may be widely disseminated through the fat of the visceral, parietal and omental peritoneum. It is frequently seen in the abdominal wall and occasionally in the fat of the thighs, the diaphragm and the pericardium. The fat splitting enzyme is thought to be carried to these distant parts by way of the lymphatics. Such a channel of spread would account for the fat necrosis seen in various parts of the abdomen where the usual direct contact with pancreatic secretion would be unlikely. A fat splitting enzyme has been found to be present in these necrotic areas.

The rôle of lipase in fat necrosis is challenged by its frequent occurrence in cases of bile peritonitis following gall bladder suppuration without pancreatic involvement, but no records can be found of the search for lipase in these instances. A mild degree of fat necrosis may clear up without leaving any trace.

Fluid in the abdomen is found in 60 per cent of cases and is usually large in amount. *Blood* is present in a varying proportion in the hemorrhagic type; *bile* is frequently found in the suppurative type.

BACTERIOLOGY

It is surprising how infrequently one sees bacteriologic studies as part of published reports of cases which have been operated upon or come to post mortem examination. This may account for the general impression that pancreatic necrosis in human beings is a sterile process. The most common organisms found in the suppurative and gangrenous types are the colon bacillus, pneumococcus, staphylococcus, and streptococcus. The most important ones, however, are the anaerobic organisms, of which one, in particular, requires special mention. This is aerogenic and similar to, if not identical with, the B. welchii. Nevertheless, it is true that the necrotic tissue is often sterile, and this is true also of the abdominal fluid. The frequent finding of B. coli and B. welchii may be due to their capacity to overgrow other organisms. It is believed that these bacteria activate the trypsinogen by the proteolytic products of their growth.

X-RAY STUDIES

The following roentgenological studies, in the order of their importance, may aid in making a diagnosis:

1. Widening of the duodenal angle due to enlargement of, or cyst formation in, the head of the pancreas.
2. Displacement of the stomach upward and the small and large intestine downward, due to cyst formation.
3. Free air in the abdominal cavity in cases of perforated ulcer.
4. Distended loops of gut with fluid levels in intestinal obstruction.
5. A cyst in the stomch area or in that of the transverse colon, sug- gesting a lesion in either of these structures, may be shown by the use of opaque media to be an extrinsic mass. Confusion may result from pressure manifestations on the stomach caused by collections of fluid in the lesser sac. These disturbances may appear as in- complete filling of the pylorus or the absence of peristaltic waves. There may also be considerable gastric residues due to partial obstruction.
6. Where there is actual inflammation, by contiguity, of the wall of the colon or stomach, further alterations in the roentgenogram will result. These developments, however, are likely to occur late in the disease. Further pressure findings may be caused by a rolled up omentum.
7. The diaphragm may be pulled down because of phlegmonous in- volvement of neighboring structures.

TREATMENT

The nature of operative procedures need not be considered here but the opinions as to immediate or delayed operation or entirely non-operative treatment may be summarized. The German literature in general seems to favor immediate operation, and many surgeons seem to agree on an early cholecystostomy so as to restore a balance in pressures of the bile and pancreatic secretion and to re-establish the outflow of the latter through its own duct. Schloffer stresses the fact that he finds the pan- creas in a poorer condition at autopsy than at the time of operation, suggesting that the process is a progressive one. However, this is to be expected if it has terminated in death, and may be explained partially by the rapid autolysis which takes place in the pancreas. Nordmann, however, pleads for conservative therapy because of the high operative mortality. He believes that the shock and other severe initial symptoms are likely to subside and, with the subsequent operation delayed, surgical risk would be lessened. He finds that the abscess or pseudocyst which develops in so many cases within two or three weeks can be drained with practically a negligible mortality. This point of view coincides with the majority of opinions of American writers. There are some who advocate urgent operation in acute cholecystitis complicated by pancreatitis.

Others urge operation on all patients whose condition shows no improvement for two weeks after the onset.

Since attacks of mild pancreatitis are prone to recur with increasing severity, once diagnosed, especially in association with gall bladder disease, operation is uniformly advised.

In a recent article Gatewood reviews the advantages and disadvantages of capsule incision, cholecystostomy for bile drainage, etc. In another, Trasoff and Scarf assemble the views of those favoring delayed operation or purely expectant treatment. Some wait until the process subsides, as is recommended by various German writers—an average delay in operation of a few days to a week. They advocate no operation whatsoever during the entire duration of the acute stage. Apparently, however, the death rate, whether the operation is immediate or only slightly delayed, is about the same. Mikkelson, a strong supporter of purely conservative treatment, reports twenty-nine cases with a mortality of only 8 per cent.

MEDICAL TREATMENT

While the medical treatment has to be symptomatic, it can accomplish a great deal in maintaining necessary functions and counteracting vicious results. Dehydration with loss of chloride must be strenuously combated. The anuria which occasionally develops should be treated with forced fluids, especially intravenous, using glucose and saline. Where there is evident disturbance in the acid-base ratio, Ringer's or Hartmann's solution should be used. Some observers strongly recommend that insulin be injected slowly with the intravenous fluid to spare the pancreas, varying the dose with the blood sugar figures. It is believed that diuresis actively maintained helps to eliminate the toxins, probably of bacterial origin, which produce the shock.

After operation on patients in whom gall bladder disease and gall stones have been found associated with pancreatitis, the subsequent diet should be carefully regulated to prevent recurrence of stones. Blood chemistry studies should be made as a check-up on the success of these measures.

The foregoing summarizes the information we have about the various factors in the problem of acute pancreatitis. The questions still unsolved, and there are many, are indicated in the various shades of opinion, particularly those relating to the etiology and the surgical phases of treatment.

ILLUSTRATIVE CASES*

The following case records are presented to show the wide variations in the clinical picture of this condition, with the resultant difficulties

in diagnosis, and to illustrate their unexplained association with other disease processes, indicating the inadequacy of our present concepts of the etiology of acute pancreatitis.

Case 1. History (Adm. 399274). A 50 year old truck driver was perfectly well until one week before admission to the hospital when he began to have generalized abdominal pains, most marked in the right lower quadrant. These pains were sufficiently severe to make the patient, a rather insensitive individual, go to bed. The pain lasted all day and was accompanied by loud borborygmi and vomiting. He felt chilly and feverish. The symptoms continued irregularly for almost a week when he began to suffer from hiccough. The latter continued with increasing severity until he entered the hospital.

Examination. The patient was well nourished. He appeared to be acutely ill. The temperature was 100.6°F. There was marked dullness over the lower third of the posterior part of the right side of the chest with diminished breath, voice sounds and fremitus. There were occasional râles over this area. The right side of the chest moved poorly in respiration. There was moderate punch tenderness over the right posterior chest and in the axilla. Pitting edema was present in the right axilla and upper portion of the right flank with slight tenderness deep in the latter area. The abdomen was soft and markedly distended. The blood pressure was 130 systolic and 90 diastolic. The pulse rate was 88 per minute.

Laboratory Data. The blood showed hemoglobin 130 per cent. It contained 24 mg. urea nitrogen, 105 mg. sugar, 0.2 mg. bilirubin, 160 mg. cholesterol, 50 mg. cholesterol ester per 100 c.c. of blood. The icteric index was 5. Fluoroscopy of the chest showed an elevated right diaphragm with definite diminution of motion in respiration. Roentgenograms showed a partial atelectasis of the right lower lobe. There was no evidence of radio-opaque gall stones.

Course. The clinical impression was a right subphrenic abscess following a ruptured retrocecal appendicitis. The patient was observed for six days during which the temperature fluctuated between 100° and 102°F. The signs at the right base persisted. The abdomen remained markedly distended in spite of effectual enemata. The right flank bulged and the pitting edema increased over this area. The punch tenderness over the flank and lower chest persisted. There was a suggestion of a smooth mass in the right upper quadrant.

At operation the greater omentum was studded with areas of fat necrosis. A small amount of free fluid was in the peritoneal cavity. A large mass, the size of a baseball, was felt near the gastrohepatic omentum, adherent to the gall bladder. Cholecystostomy was performed. The subphrenic space was found to be absolutely clear. Four days afterward the patient developed pain in the left chest and a friction rub over the left

lower lobe. Later, dullness and bronchial breathing appeared. The temperature fluctuated between 101° and 104°F. and the breathing became labored and rapid. The patient died suddenly.

Necropsy Findings. Extensive sloughing and fat necrosis of the pancreas and a widespread retroperitoneal phlegmon were found. The head of the pancreas, which was particularly involved, was surrounded by necrotic tissue. The gall bladder showed chronic inflammatory changes and contained gall stones. There was an embolism in the left pulmonary artery. Masses felt were found to be rolled up omentum studded with fat necrosis, and the swollen head of the pancreas.

Comment. This case is an illustration of a retroperitoneal phlegmon simulating a perinephric abscess. Diaphragmatic and chest signs suggested a subphrenic abscess, but these were actually due to an extension of the retroperitoneal condition. However, the presence of an associated intraperitoneal process should have suggested acute pancreatitis.

Case 2. History (Adm. 363705). A 70 year old male who, four years previously, had had an amputation of the leg because of arteriosclerotic gangrene, had been fairly well since then except for occasional attacks of precordial pain which radiated to the left shoulder. One week before admission to the hospital he began to experience severe epigastric distress after meals. Fifteen hours before admission he was awakened by an agonizing pain in the epigastrium. This radiated to the right shoulder, right upper quadrant and back. He became pale, broke out in a cold sweat and then vomited.

Examination. The patient was in a state of moderate shock, was dyspneic and slightly cyanotic. There was some dullness and diminished breath sounds at the right base of the chest. The abdomen was markedly tender and the wall was diffusely spastic. The blood pressure was 160 systolic and 105 diastolic. The temperature was 100°F. An abdominal puncture was done in the left lower quadrant, and a small amount of fluid obtained which contained a moderate number of pus cells but no organisms.

Course. The diagnosis rested between a perforated gastric lesion and acute cholecystitis, although pancreatitis was suggested because of the presence of shock, cyanosis and dyspnea. The poor condition of the patient necessitated conservative treatment. Intravenous fluids were administered. The blood amylase taken on admission was reported at 40 units; the peritoneal fluid contained diastase but no trypsin. The temperature rose gradually to 106°F. and the patient died on his second day in the hospital.

Necropsy Findings. Acute pancreatitis with fat necrosis of the omentum and peritoneum was present. Stones in the gall bladder and bile ducts were found. In addition the gall bladder wall was perforated. Acute peritonitis, coronary artery sclerosis with marked narrowing and myocardial fibrosis were also found.

Comment. This is a typical example of acute pancreatitis in an old man with gall bladder disease, complicated by rupture of the gall bladder and peritonitis.

Case 3. History (Adm. 399595). A 20 year old German Jewess was said to have had glycosuria for six months. Twenty-four hours prior to her admission to the hospital she began to experience severe abdominal pain requiring the administration of morphine. Three hours before admission the patient lapsed into coma.

Examination. The patient was comatose and showed marked hyperpnea. The eyeballs were extremely soft. The skin was cold and several xanthomata were seen on the dorsa of both hands. The temperature was 97.2°F; the pulse rate was 140 per minute; and the respiration rate was 40 per minute. The blood pressure was 130 systolic and 80 diastolic. Lungs were clear, heart not enlarged. The abdomen was soft, slightly distended but there was no tenderness or rigidity.

Laboratory Data. The blood had a hemoglobin of 110 per cent. There were 450 mg. of sugar, 15 mg. of urea nitrogen, 1250 mg. of cholesterol,— each per 100 c.c. of blood. The carbon dioxide combining power was 6 volumes per cent. There were 61,000 white blood corpuscles per cubic millimeter of blood of which 88 per cent were polymorphonuclear neutrophiles. The urine contained 4 per cent sugar and 2 plus acetone.

Course. Three thousand cubic centimeters of saline and Hartman's solution were given intravenously, together with 350 units of insulin in the twelve hours the patient remained alive. Despite this intensive therapy the blood sugar remained at 400 mg. per 100 c.c. and the carbon dioxide combining power at 9 volumes per cent. The urine, however, showed 2.5 per cent sugar and only a trace of acetone. The patient went into shock, the blood pressure dropped to 85 systolic and 25 diastolic. Urinary output fell to a minimum. The temperature rose to 105°F. before the patient died.

Necropsy Findings. Subacute pancreatitis was found.

Comment. This was a case of severe diabetic coma in a young girl who did not respond to apparently adequate and intensive therapy. The finding at post mortem examination clarified the obscure clinical features.

Case 4. History (Adm. 365522). A 60 year old Porto Rican female experienced episodes of epigastric distress associated with nausea and vomiting for two months. The discomfort or pain accompanying this radiated to the right upper quadrant. Four days before admission she had a severe attack consisting of upper abdominal pain and vomiting. This was soon followed by marked abdominal distention.

Examination. The patient was acutely ill. The heart and lungs were negative. The abdomen was greatly distended. There was diffuse tenderness which was especially marked in the right upper quadrant and epigastrium.

Course. An abdominal puncture was done in the left lower quadrant and some clear light brown fluid was obtained. No organisms, and only an occasional pus cell, were found. The temperature rose to 102°F. In the left upper quadrant there was resistance and tenderness to palpation. The left flank became boggy. A second abdominal aspiration was done three days after admission and this yielded typical brownish beefy fluid. The pain then shifted to the right upper quadrant. Five days later a spherical mass was felt in this area, and could be distinguished as apart from the liver. Acute pancreatitis was diagnosed and operative interference was thought advisable.

Operation. Only a little free peritoneal fluid was seen. The entire omentum was studded with pin-head to millet seed sized areas of fat necrosis, some of which were calcified. The gall bladder was not acutely inflamed but contained 40 c.c. of sandy bile. No gall stones were present. A cholecystostomy was performed.

The temperature after the operation continued to be elevated. On the seventh postoperative day the patient complained of pain over the left lower chest where a friction rub was heard. On the tenth day a friction rub, dullness and diminished breath sounds appeared at the right lower lobe. The next day the patient suddenly died.

Necropsy Findings. Acute suppurative pancreatitis with abscess formation, diffuse fat necroses of the peritoneum and omentum, and chronic cholecystitis with a dilated common bile duct were present. In addition, there was an infarct in the lower lobe of the right lung due to an embolus in the pulmonary artery, a diverticulum of the duodenum and phlebitis of the splenic vein.

Comment. This case is illustrative of recurrent mild attacks of acute pancreatitis during a period of two months. The presence of gall bladder disease, without gall stones, is probably not etiologically associated with the pancreatitis. It was the duodenal diverticulum above and behind the ampulla of Vater which, by obstructing the outflow, caused the dilatation of the common bile duct and the subsequent acute pancreatitis. The diagnosis in this instance was made with the aid of the examination of the abdominal fluid obtained by paracentesis. The associated phlebitis of the splenic vein might have given rise to splenomegaly (splenomegalic syndrome), had the patient recovered.

Case 5. History (Adm. 398214). A 60 year old Irish woman was known to have been an habitual drunkard for fifteen years, and to have passed through an episode of delirium tremens five years before. Six days before admission she felt weak and went to bed. She had frequent nose bleeds. On the day of admission she vomited a large amount of blood.

Examination. The patient was stuporous and vomited blood occasionally. Dilated veins were visible on the chest and a typical caput medusae was present around the umbilicus. The heart was enlarged to the left

and a systolic murmur was heard at the apex. The abdomen was soft and distended. Dullness in the flanks was present and a fluid wave could be elicited. There was felt "a very large, hard, irregular mass, freely movable, in the right upper quadrant, distinct from the liver, which was palpable above it. Other smaller, softer masses were felt to the left of the umbilicus."

Laboratory Data. The blood pressure was 120 systolic and 50 diastolic. The hemoglobin was 65 per cent. The blood urea nitrogen was 125 mg., the sugar, 205 mg., the bilirubin was 2.5 mg., and the cholesterol was 125 mg.,—each per 100 c.c.; there was a trace of cholesterol ester. The icteric index was 12. The urine did not contain any bile. The urobilin dilution was one to forty.

Course. The diagnosis of an intra-abdominal neoplasm was made, a primary carcinoma of the liver (on the basis of a Laennec's cirrhosis) with peritoneal metastases being considered most probable. The patient never recovered consciousness. The temperature rose rapidly to 104°F. and she died three days after admission.

Necropsy Findings. There was an acute diffuse pancreatitis with fat necroses of the mesentery, omentum, gall bladder and intestinal serosa, retroperitoneal and perirenal fat. In addition there was cirrhosis of the liver, splenic vein thrombosis with splenic congestion and a ruptured varix of the esophagus.

Comment. This case shows the association of cirrhosis of the liver with acute pancreatitis in an old alcoholic, which probably followed an alcoholic debauch. Masses in the abdomen were simulated by rolled up omentum involved with fat necrosis.

Case 6. History (Adm. 365915). A 54 year old male had been treated in the hospital two months prior to his last admission for vesicle calculi. At that time the presence of hypertension, hypertrophy of the prostate and left renal calculi was noted. Since his discharge the patient suffered from weakness, dyspnea and left upper quadrant pain, associated with almost continuous singultus. He had been in bed.

Examination. The heart was found to be enlarged to the left. There was a large mass in the left upper quadrant which extended to a point 4 cm. below the costal margin. This was firm, smooth and very tender and was considered to be a hydronephrosis due to a calculus.

Laboratory Data. The urine showed a trace of albumin and contained a few white blood cells. Chemical examination of the blood gave normal results.

Course. The temperature became spiking in character rising to 102°F. Roentgenographic examination with the aid of a barium enema showed a partial obstruction of the sigmoid colon at its mid-portion, due to an extrinsic mass. Intravenous and retrograde pyelograms indicated but slight dilatation of the pelvis and calyces of the left kidney, with a calculus

within the pelvis. This excluded the kidney as the explanation for the abdominal mass. An exploratory laparotomy was done exposing a large, fluctuant retroperitoneal mass which occupied the position of the body of the pancreas. Marsupialization was done. Five days later the mass was incised and drained. The evacuated pus was foul smelling and yielded a streptococcus viridans when cultured. The course from then on was progressively downhill. He developed bronchopneumonia. The blood urea rose to 65 mg. per 100 c.c. and he died on the sixth postoperative day.

Necropsy Findings. Necropsy revealed an abscess and necrosis of the body and tail of the pancreas, perforation through the mesentery with extension to the left periadrenal region and fat necroses of the peripancreatic fat, greater omentum, mesentery and adrenal fat tissue. In addition there was a calculus in the left renal pelvis, cortical abscesses in the left kidney, chronic pyelitis, left ureteritis, cystitis, a hypertrophied prostate gland and a bronchopneumonic process in both lower lobes. The gall bladder was normal both upon gross and microscopic examination.

Comment. The abscesses and necrosis in the pancreas, in the absence of gall bladder disease, were probably hematogenous in origin. The formation of a pseudo-cyst, the nature of which was obscure clinically and which simulated a renal mass was unusual. The suppurative process in the pancreas extended through the mesentery to the retroperitoneal area and irritated the diaphragm, thus explaining the singultus. The normal blood urea content and the complete absence of the so-called typical picture of acute pancreatitis are other unusual features.

Case 7. History (Adm. 39909). The patient was a 30 year old male who six months before had had the right testis removed because of a neoplasm. On the night preceding admission he indulged in an alcoholic debauch. The following morning he awoke with upper abdominal pain of a colicky nature. He felt nauseated and vomited frequently. The pain increased in severity and was most marked above the umbilicus. The vomitus became coffee brown in color.

Examination. The patient was an obese and acutely ill young man. The temperature was 99°F. The pulse rate was 90 per minute. The blood pressure was 120 systolic and 80 diastolic. There was moderate tenderness, not "rebound", in both upper quadrants. The heart and lungs were negative.

Laboratory Data. The urine contained a trace of albumin, 1.5 per cent sugar and showed a 3 plus acetone reaction. There was no bile and the urobilin dilution was 1 to 20. A few casts were seen. The blood contained 0.4 mg. of bilirubin, 18 mg. of urea nitrogen, 280 mg. of sugar, 310 mg. of cholesterol and 35 mg. of cholesterol ester per 100 c.c. The icteric index was 4.

Course. The vomiting of coffee brown material continued. This showed a positive reaction to the guaiac test. The tenderness in the

right upper quadrant persisted and a resistence of the entire abdominal wall appeared. The temperature rose to 103.6°F. An exploratory laparotomy was done revealing diffuse fat necroses of the omentum and a palpable mass in the region of the second portion of the duodenum. During the operation the patient became cyanotic, the pulse thready and the breathing labored. A transfusion was done. The temperature later rose to 105°F. The patient died four hours afterward.

Necropsy Findings. These were: an acute hemorrhagic pancreatitis, fat necroses of the omental, peritoneal, peripancreatic, diaphragmatic and pericardial fat, a dissecting hematoma of the second and third portions of the duodenum and retroperitoneal tissues, a hemoperitoneum, a hemopericardium and a right hemothorax.

Comment. The acute pancreatitis found after alcoholic excess was mistaken for a simple alcoholic gastritis. The presence of hyperglycemia and glycosuria in acute pancreatitis should be noted. The persistent vomiting of coffee brown, guaiac positive material was due to high intestinal obstruction. This, in turn, was caused by the dissecting hematoma around the second and third portions of the duodenum. The occurrences of a hemopericardium and hemothorax were unusual. The extra-abdominal fat necrosis, i.e., pericardial, was probably due to lymphatic extension.

Case 8. History (Adm. 354514). A 44 year old man had been complaining for one year of epigastric distress and fullness after eating, especially when the meals consisted of fatty food. Two weeks before admission to the hospital he was seized with severe cramp-like pains which radiated to the right lumbar region and to the angle of the right scapula. This was associated with vomiting. The temperature was said to have been 102°F. Later the pain radiated to both lower quadrants. The urine became dark and the skin yellowish. Shortly before admission there was a recurrence of short colicky pains around the umbilicus, and the jaundice became more evident.

Examination. The patient was obese and his skin and sclerae were icteric. There was bilateral costo-vertebral tenderness. The abdomen was distended uniformly and an indistinct mass was felt about four fingerbreadths above the umbilicus. Examination of the lungs and heart was normal. The temperature was 102°F.

Laboratory Data. The urine contained bile and a few pus cells. The blood contained 11 mg. of urea nitrogen, 100 mg. of sugar, 180 mg. of total cholesterol, 60 mg. of cholesterol ester, 2 mg. of bilirubin,—each per 100 c.c. The icteric index was 25. The blood amylase was 25 units. Two attempts to visualize the gall bladder roentgenographically failed.

Course. A diagnosis of acute pancreatitis was made, and exploratory laparotomy was carried out. This showed the presence of fat necrosis in the transverse mesocolon and omentum. The pancreas was enlarged, firm and similarly studded with fat necrosis. The gall bladder appeared

to be normal and no calculi could be palpated either in it or in the common
bile duct.   An appendectomy was performed.   Thereafter, the tempera-
ture rose to 102° and 103°F, then gradually fell to normal in five days.
The icteric index increased to 75 and later decreased to 14; the blood
amylase fell to 8 units.   The patient progressed favorably and was
discharged well.   He has been followed for four years and has remained
in good health.

Comment.   This is a case of acute pancreatitis with jaundice which
could not be explained by the presence of gall stones.   The other features
were typical.

Case 9.   History (Adm. 401503).   A young woman, aged 23 years, was
well until three months before admission to the hospital.   While in the
seventh month of a normal pregnancy, she was seized with a sharp,
pressing pain in the left anterior axillary line.   The pain radiated across
the chest to the precordium, left shoulder and neck.   It persisted with
somewhat diminished intensity for two days when the patient had a
miscarriage.   Since then attacks of pain had recurred frequently, chiefly
in the left upper quadrant, associated with nausea and vomiting.   Jaun-
dice was not noted.   Occasionally she felt feverish and chilly.   Five
days before admission she again experienced a very sharp, knife-like pain
in the lower part of the left side of the chest.   She stated that she had
noticed a mass in the epigastrium during the preceding three months.
She had lost fifty-five pounds in weight and became progressively weaker
during this period.

Examination.   The temperature was 100.6°F.   The blood pressure was
106 systolic and 70 diastolic.   A soft systolic murmur was heard over the
precordium.   The abdomen was moderately distended, and a large, very
tender, soft mass was felt filling the entire epigastrium and extending to
the level of the umbilicus.   It moved with respiration.

Laboratory Data.   The blood contained 70 per cent hemoglobin.   The
icteric index was 7.   The total cholesterol in the blood was 190 mg. per 100
c.c., with a trace of cholesterol ester.

Course.   Two days after admission the temperature rose to 102.2°F.
and the pulse rate to 140 per minute.   She complained of severe pain
in both upper quadrants.   Generalized abdominal and marked rebound
tenderness were present.   It was felt that there had been a rapid extension
of the original inflammatory process to adjacent parts of the peritoneal
cavity and that an exploratory laparotomy was advisable.   This was
carried out and about two quarts of chocolate-colored fluid were obtained
from the general peritoneal cavity.   A small tear was seen in the trans-
verse mesocolon, through which a large amount of similarly colored fluid
was issuing.   Gangrenous tissue was found in the lesser sac and fat
necrosis in the omentum. . A biopsy of a piece of the omentum confirmed

the impression of necrotic fat tissue and also showed evidences of acute inflammation. The gall bladder appeared to be normal. After the operation the patient improved. Drainage from the wound continued for some time. The fluid from the peritoneal cavity contained diastase, but no trypsin.

The patient was discharged on the twenty-fourth postoperative day. She has been followed for one year and is perfectly well. X-ray studies of the gall bladder did not reveal any stones.

Comment. The occurrence of acute pancreatitis during pregnancy is unusual. In this instance the process subsided and a pseudo-cyst of the lesser sac had formed which finally ruptured into the general peritoneal cavity.

Case 10. History (Adm. 403220). A 48 year old man discovered the presence of jaundice, pruritis and clay-colored stools about one month before entering the hospital. Two weeks later his stools became brown, but the jaundice persisted. There was a tendency to bleeding (epistaxis and ecchymosis). At no time was there any abdominal pain.

Examination. The patient was well nourished and had a deep icteric tinge to his skin. The abdomen was soft and the liver edge was firm and extended two fingerbreadths below the right costal margin. The spleen reached the same distance below the left costal margin. The lungs and heart were negative.

Laboratory Data. The urine gave a two plus positive bile reaction, and the urobilin content was 1 to 10. Tyrosine was absent. The stools were brown and gave positive reactions to both urobilin and guaiac. The blood hemoglobin percentage was 97; the icteric index was 60, bilirubin 14 mg., and the Takata-Ara reaction was negative. In addition the blood contained 22 mg. of urea nitrogen, 105 mg. of sugar, 190 mg. of cholesterol, a trace of cholesterol ester, 5.3 mg. of total protein of which 3.9 was albumin and 1.4 was globulin,—each per 100 c.c.

Course. The patient appeared to be suffering from an ordinary case of toxic hepatitis. Five days after admission the abdomen became markedly distended and a small amount of ascites and dependent edema were noted. He became mentally sluggish and vomited several times. The icteric index dropped to 40 and the bilirubin content to 12 mg. per 100 c.c. of blood. The urine showed a small amount of tyrosine. In spite of transfusions, intravenous administration of glucose solution and the use of liver extract, the patient became comatose and died thirteen days after admission.

Necropsy Findings. Acute yellow atrophy of the liver, acute pancreatitis with fat necrosis and intestinal hemorrhage were found.

Comment. The occurrence of acute pancreatitis in the course of acute yellow atrophy, with total absence of pain, should be noted.

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CORONARY ARTERY THROMBOSIS AS A DELAYED POSTOPERATIVE COMPLICATION

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It is well known that persons with arteriosclerosis of the coronary arteries are poor surgical risks, that they show an unexpected operative mortality of 8 per cent (1). Most of these excess deaths are due to coronary thrombosis, or to acute myocardial ischemia in the presence of diseased coronary arteries without actual occlusion. It has become an accepted practise to subject patients with coronary artery disease to operation only when the indications are compelling

Since coronary thrombosis occurs so commonly during sleep or rest, the idea has often been expressed that the development of a coronary artery occlusion after an operation represents only a fortuitous coincidence, that the operation and anesthesia, as such, are not the precipitating agents. It is difficult to prove a causal connection, but clinical experience suggests that surgical procedures may induce coronary artery thrombosis (2).

In certain instances it seems clear that the trauma of the operative experience actually brings on thrombosis in a coronary artery, as in the case reported by De Santo (3) of a man who died twelve hours after a herniorraphy done under spinal anesthesia. At autopsy there was found a hemorrhage into the peritoneum due to injury of an artery during the operation, as well as a fresh thrombus in one of the coronary arteries. Although it is distinctly uncommon to see coronary thrombosis directly provoked by the physical and emotional strain of operation and anesthesia, the surgeon, when operating on a patient with coronary artery disease, must be unusually painstaking to avoid traumatism, hemorrhage and shock. The underlying surgical disease, infection, with possible dehydration, starvation and general asthenia may be responsible for inducing a coronary thrombosis.

Most postoperative coronary artery thromboses occur from the fifth to the fifteenth day after operation, often at a time when the patient seems fully convalescent, resembling in this respect postoperative pulmonary embolism (4). Severe traumatic injuries may be followed by coronary thrombosis after a similar time interval. It has been pointed out that cerebral thrombosis, too, may occur postoperatively at about this period (3). The cases of postoperative coronary thrombosis that I have ob-

served in my practise have all occurred from one to two weeks after operation.

Case 1. A man 51 years of age was first seen in September 1933. He had had a herniorraphy six years previously at the age of 45. Two weeks after the operation, on leaving the hospital, he noted, while walking, trembling sensations in the forearms which radiated to the chest where they were experienced as a cramp which compelled him to halt. Similar anginal pain on exertion has persisted ever since. In 1933 the attacks became quite severe, lasting fifteen minutes and being associated with marked sweating. He was unable to walk more than half a block. Physical examination and the electrocardiogram were negative. In 1937, the subjective and objective findings were unchanged.

Although this patient does not present classical evidences of coronary thrombosis, he developed his symptoms suddenly two weeks after operation. It is probable that when angina pectoris appears suddenly, and persists, its onset is determined by a sudden organic change in one of the coronary arteries, usually a coronary thrombosis.

Case 2. A man 45 years of age was first seen in September 1937. He had had symptoms of angina pectoris for eight years, from the age of 37. On August 15, 1937 he was subjected to an operation for prolapse of the rectum, under ether anesthesia. The operation and the postoperative course were uneventful. On August 26 he complained of feeling completely exhausted. This persisted for two days. On August 28 he had severe pain in the lower chest, radiating from front to back and lasting five hours. The attack commenced shortly after dinner. The following day he felt better except for intensification of the pain after eating. He stayed in bed all week and then travelled to my office. The significant findings on examination were: a dull first heart sound; blood pressure, systolic 90, diastolic 55. The electrocardiogram showed Q waves with negative cove plane T waves in leads II and III, and a very deep T wave in lead IV. It was clear that he had had an infarction of the posterior aspect of his left ventricle, occurring thirteen days after operation.

Case 3. A man aged 44 was first seen in May 1933 during an attack of coronary thrombosis, from which he made a good recovery. He had a huge left ventricle, and a blood pressure ranging from 250 systolic and 140 diastolic to 200 systolic and 110 diastolic. After about four months he returned to his work to continue as an operator in a factory, in spite of typical angina pectoris on exertion. In May 1936 he developed an acute appendicitis for which he was operated on. Convalescence was uneventful. On the ninth postoperative day, he developed severe precordial pain which radiated to the left shoulder and arm. A pleural friction rub was heard in the left axilla. His temperature rose to about

101°F. The following day râles were heard at the bases of both lungs. Late that evening he was again seized with severe precordial pain, which radiated down the left arm. His pulse rate was 140 per minute; it was quite irregular. Twenty minutes later he died very suddenly. The electrocardiogram taken on admission to the hospital showed what it had shown before, namely, negative T waves in all leads. On the day of his death the T waves in leads II and III had become upright.

It is unlikely that these late coronary thromboses following operation are chance occurrences. Master's (5) observation that coronary closures rarely develop while a patient is in a medical ward, but that they are not uncommon in the surgical wards is suggestive. It seems probable that the same factors that determine other postoperative arterial and venous thromboses, in particular the factors that determine venous thrombosis and pulmonary embolism are responsible for these delayed coronary thromboses. Statistics show that postoperative venous thrombosis and pulmonary embolism occur most commonly between the third and eighth day following operation, but that they may occur after several weeks have elapsed (6, 7). The causes of postoperative thrombosis remain obscure, although certain evidence points to an increase in the number of platelets and of fibrinogen in the blood (8). Be that as it may, it is likely that the tendency to intravascular clotting usually manifested in the veins may, in the presence of arteriosclerotic coronary arteries, favor the development of coronary thrombosis.

The diagnosis of postoperative coronary thrombosis is often difficult. Pain may be absent or minimal. Not uncommonly pulmonary embolism is mistaken for coronary thrombosis (9). Pulmonary embolism is characterized by the sudden onset of shock, faintness, pallor, sweating, rapid pulse, fall in blood pressure and vomiting (10, 11). Dyspnea may be absent. Hemoptysis, pleural friction rub, and signs of pulmonary consolidation may not appear for a day or two, or may never become manifest. Even a roentgen film of the lungs may show no lesion. Cyanosis and dyspnea are more common in pulmonary embolism, substernal or precordial pain in coronary thrombosis. When pain occurs in pulmonary embolism it is usually felt in the axillae and is often exaggerated by inspiration. Electrocardiography often aids in the differential diagnosis. Acute pulmonary embolism is followed by electrocardiographic changes which superficially resemble those of coronary thrombosis. They are characterized by a prominent S wave in lead I, a depressed ST segment, at times with a diphasic T wave in lead II, a slightly elevated RT segment and a negative T wave, and a prominent Q wave in lead III, and an upright T wave in lead IV. There is further difficulty in differentiating between pulmonary embolism and coronary thrombosis because fully one-half of all cases of venous thrombosis and embolism occur in patients with damaged hearts (12).

The difficulty in differential diagnosis is well illustrated by the following case:

Case 4. A woman aged 51 was first seen in April 1933, complaining of cough and asthmatic breathing. This was due to a large substernal thyroid gland. General examination and the electrocardiogram at that time were negative. Blood pressure was 130 systolic and 85 diastolic. She was seen again in January 1937. Her pulmonary symptoms, due to compression of the trachea by the thyroid, had become so severe that she was referred for operation. An electrocardiogram at this time was also normal. On January 13, eight days after her operation, while at home, she experienced excruciating pain in the right lower chest and became quite dyspneic. The following day, and again the day after, she had still greater pain in the left chest and the temperature rose to 101°F. There was diminished breathing with crepitant râles at the left base. The heart showed gallop rhythm. The blood pressure was 90 systolic and 60 diastolic. The electrocardiogram showed a slurred QRS with negative cove plane T waves in leads II and III, and a positive T wave in lead IV. The S wave in lead I was small. X-ray examination showed an infiltration in the axillary region of the right lung. On February 1 she suddenly developed severe pain in the right chest, which radiated to the right shoulder, and lasted about twenty hours. On February 2 her temperature rose to 100.6°F. The pulse rate was 120 per minute; respirations 24. The blood pressure was 120 systolic and 80 diastolic. There was no dyspnea. A few crackling râles were heard at the right base and there was tenderness in the right upper quadrant. The heart showed gallop rhythm. The electrocardiogram was unchanged. On February 5 she complained of pain below the right scapula, which was worse on breathing. There was some dullness at the right base, but no râles. The heart sounds were muffled and there still was gallop rhythm. Roentgen film of the chest showed bilateral hilar infiltrations, suggesting adenopathy and a small shadow at the right base. On this day she developed auricular flutter, which was demonstrated on the electrocardiogram. Two days later normal sinus rhythm had been restored, and the electrocardiogram resembled the one taken after her first attack of pain. The blood pressure was 94 systolic and 74 diastolic. On February 11 she complained of persistent precordial pain. She died very suddenly four days later without having complained of further pain.

In this case the repeated episodes of chest pain and the lung signs and the roentgen findings suggest that she had repeated pulmonary emboli, although pulmonary embolism is very rare after thyroid operations. The persistent gallop rhythm and the persistent electrocardiographic findings are not wholly characteristic of pulmonary embolism, and suggest that she had a coronary thrombosis as well.

SUMMARY

In persons with arteriosclerosis of the coronary arteries coronary thrombosis rarely occurs during or immediately after the operation, unless there has been much hemorrhage or shock. Coronary thrombosis often occurs from one to two weeks after the operation. Postoperative venous thrombosis occurs after a similar time interval. It seems probable that postoperative coronary and venous thromboses are due to the same underlying causes. Because of the resemblance in symptomatology and similarity in time of occurrence, it is difficult to distinguish postoperative pulmonary emoblism from coronary thrombosis.

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PSOAS MUSCLE ABSCESS SIMULATING PERINEPHRITIC ABSCESS

Report of Two Cases

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The early diagnosis of the metastatic type of perinephritic abscess is very often a perplexing problem, in spite of the many diagnostic aids at our disposal. The difficulty is frequently due to a paucity of clinical signs and symptoms or to the location of the abscess. An abscess near the upper pole of the kidney may simulate a subphrenic or intrathoracic lesion. If mesial or anterior it may be confused with an intra-abdominal condition. The most common site is posterior to the kidney. Here difficulty arises from the fact that lesions in structures adjacent to the kidney area can give identical signs and symptoms. It is to emphasize this possibility and the importance of an early and thorough exploration that the following cases are reported.

Case 1. History (F. C., Adm. 396440). The patient, male, aged 8, was admitted to the surgical service on July 29, 1936 with a five day history of pain in the right loin associated with fever, lassitude, and wakefulness. During the preceding three weeks he had had a series of furuncles about the chest, abdomen, and extremities. He had an attack of right loin pain with fever and difficulty in walking about one year before this admission, which subsided spontaneously at the end of one week.

Examination. The child appeared well nourished, apathetic, temperature 101.4°F., pulse 104 per minute, and respirations 22. The skin presented recent and healed furuncles over chest and legs. Culture of pus from a fairly recent one showed staphylococcus aureus. The right abdominal muscles were held rigid and he was tender over the right costovertebral angle.

The urine was negative except for the presence of an occasional white blood cell and the stained sediment showed gram positive cocci and gram negative diplococci.

The blood count showed 13,450 leucocytes of which 78 per cent were polymorphonuclears. The hemoglobin was 68 per cent. The blood Wassermann was negative. Urea nitrogen was 10 mgm. per 100 cc. The phthalein output was 65 per cent within two hours.

An excretory urogram failed to show any abnormality in the upper urinary tract. A ring-shaped calcific shadow was seen in the right upper quadrant of the abdomen definitely extra-urinary, believed to be a gall stone or calcified gland. There was obliteration of the right psoas muscle margin and curvature of the lumbar spine with the convexity to the left and definite narrowing of the right costo-iliac space (Fig. 1).
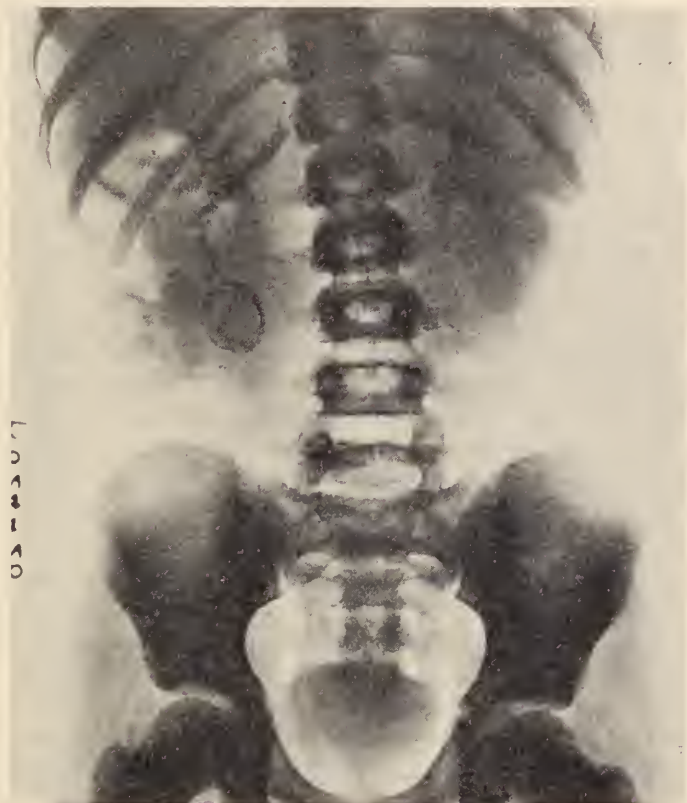
FIG. 1. Excretory urogram showing curvature of the lumbar spine with convexity away from the diseased side and definite narrowing of the right costo-iliac space; obliteration of the right psoas muscle margin. The extra-renal ring-shaped shadow on the right side is interpreted as calcified gland.

Course. The patient was observed for forty-eight hours during which time the temperature varied from 99.6°F. to 102°F. and the right costovertebral tenderness persisted. A diagnosis of cortical abscess of the right kidney with perinephritis or perinephritic abscess was made and exploration advised.

On July 31, 1937, through a right lumbar incision, the kidney was exposed and failed to show any evidence of suppuration. The perinephric fascia (Gerota's) overlying the quadratus lumborum and psoas muscle

appeared somewhat edematous. This was stripped mesially and a bulging psoas muscle was exposed showing deep fluctuation. Aspiration revealed thick pus from which staphylococcus aureus was recovered on culture. The muscle was opened bluntly, pus evacuated, and the abscess cavity drained. Digital exploration of the cavity failed to show any bare bone.

The postoperative convalescence was uneventful, temperature reaching normal on the fifth postoperative day, and remaining so up to the date of discharge. A postoperative X-ray examination of the spine taken August 17, 1936, approximately three and a half weeks after the onset of symptoms, failed to show any abnormality in the spine. The patient was discharged from the hospital August 20, 1936, the wound completely healed.

Follow-up. The patient has been seen several times since leaving the hospital and found in excellent condition. An X-ray examination made December 5, 1936 showed the calcified shadow unchanged. The psoas muscle margins were clear.

Case 2. *History* (J. F. C., Adms. 404447, 405363). The patient, male, aged 42, a salesman by occupation, was admitted to the medical service of Dr. B. S. Oppenheimer on February 9, 1937. Two weeks prior to admission he suddenly had a severe *chill* lasting about an hour and a half, temperature reaching 105°F., followed by profuse sweating. His physician diagnosed the condition as pneumonia or influenza. The following day he began to have pain in the parumbilical region and right upper abdomen. The pain subsided and the temperature reached normal after about five days. Two days later he began to have a low-grade fever ranging from 99° to 102.5°F. with profuse sweats, leucocytosis 20,000, and colicky pains referable to the right upper abdomen and right kidney region. These symptoms persisted up to the time of admission. The urine showed a trace of albumin but was otherwise negative.

Examination. The patient appeared well developed, fairly comfortable, temperature 100°F., pulse 80 per minute, respirations 20. He complained of pain in the right upper abdomen and had marked right costo-vertebral tenderness.

The urine was clear, showed a very faint trace of albumin and an occasional white blood cell. Staphylococcus albus was recovered on culture.

The blood count showed 16,150 leucocytes of which 68 per cent were polymorphonuclear neutrophiles. The hemoglobin was 90 per cent. The blood Wassermann was negative. Urea nitrogen was 12 mgm. per 100 c.c. An X-ray examination of the abdomen with special reference to the gall bladder region was negative. The Graham test showed good visualization. An excretory urogram showed an apparently normal urinary tract.

The temperature rose to 101°F. the following day but returned to normal within twelve hours, and remained so for the subsequent six days.

The pain and tenderness disappeared. The patient left the hospital February 16, 1937, symptom-free, without a definite diagnosis. He remained well for one week and then chills and fever returned together with severe pain in the epigastric region which subsequently became localized to the right costo-vertebral angle. He was re-admitted to the hospital March 4, 1937, having had a severe chill the day before.

Re-examination. The patient appeared fairly comfortable, temperature 102°F., pulse 102 per minute, respirations 24. The lower pole of the right kidney was definitely palpable and he was markedly tender over the right costo-vertebral angle.

The leucocyte count at this time was 21,300, 65 per cent polymorphonuclear neutrophiles. The hemoglobin dropped to 81 per cent. An excretory urogram on March 5, 1937 showed a normal upper urinary tract. The right ureter appeared tortuous and somewhat displaced laterally. There was some clouding of the right psoas muscle shadow, definite curvature of the lumbar spine, with the convexity to the left and narrowing of the right costo-iliac space (Fig. 2).

He was seen by Drs. Edwin Beer and A. Hyman in consultation, who suspected the presence of a cortical abscess of the kidney with perinephritis. While under observation on the medical service for about three weeks, various X-ray studies were made with negative results. He continued to run a septic temperature with daily fluctuations from 99.4°F. to 104°. Repeated blood cultures were negative. The hemoglobin gradually dropped to 67 per cent and in spite of a blood transfusion the patient appeared to be definitely and rapidly losing ground.

Cystoscopic examination, including retrograde pyelography, by Dr. A. Hyman on March 25, 1937 failed to reveal any abnormality in the urinary tract. The specimens from both kidneys showed good function, the right contained an occasional white blood cell, and both were reported sterile. A diagnosis of cortical abscess of the right kidney with perinephritis or perinephritic abscess was made and surgical exploration advised.

Course. On March 26, 1937, after approximately three weeks' observation, the right kidney was exposed through a lumbar incision with negative findings. After complete mobilization and inspection of the kidney, including decapsulation, it was displaced forward and mesially, protected with gauze, and the psoas muscle exposed. This was found indurated, irregular, and the overlying Gerota's fascia intimately adherent to it. A blunt opening was made into the muscle and about three to four ounces of thick creamy pus liberated. A hemolytic streptococcus was recovered on culture. Digital exploration of the abscess cavity revealed a denuded transverse lumbar process corresponding to about the level of the hilus of the kidney. The abscess cavity was packed with iodoform gauze and a rubber dam placed between it and the kidney. The anterior two-thirds of the incision was closed in layers.

The postoperative convalescence was remarkably smooth. The tem-

perature gradually reached a normal level and he was discharged from the hospital on April 17, 1937, the twenty-second day after operation, the wound completely healed except for a small discharging sinus at the posterior angle.
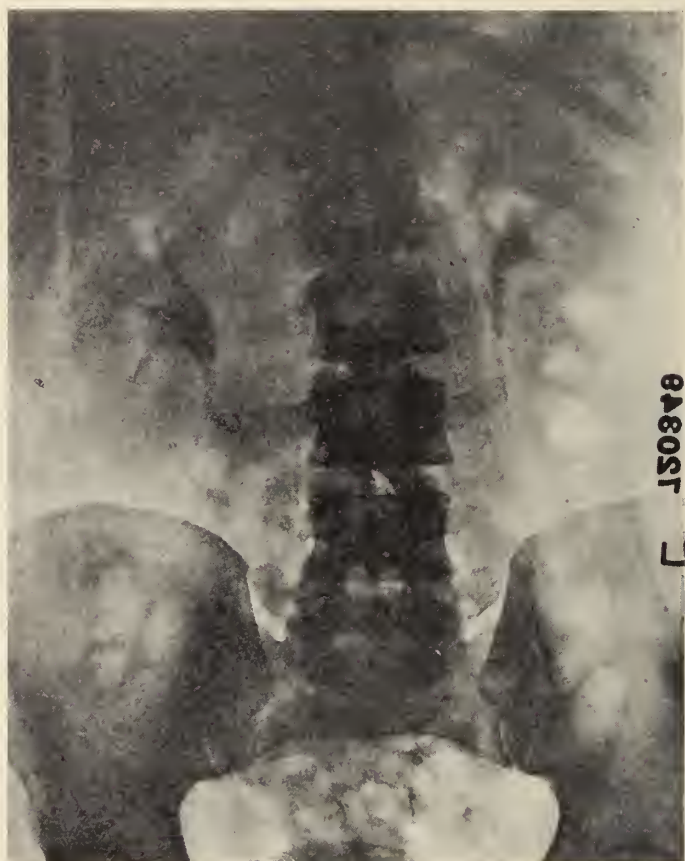
Fig. 2. Excretory urogram showing curvature of the lumbar spine with convexity away from the diseased side and definite narrowing of the right costo-iliac space; clouding of the right psoas muscle.

Follow-up. The sinus closed within a few weeks after leaving the hospital. When last seen August 7, 1937 he was in excellent condition, back at work, and with no complaints.

<div align="center">COMMENT</div>

The diagnosis of perinephritic abscess was based in each case on the following evidence:

1. Pain in the kidney region with muscle spasm and persistent costo-vertebral tenderness.

2. Fever and prolonged toxemia of unexplained origin with leucocytosis and increase in polymorphonuclear cells.

3. Negative urinary findings except for the presence of cocci in the centrifuged stained sediment.

4. The history of recent furunculosis in the first case and possibly the influenza infection in the second.

5. The positive roentgenographic evidence in the absence of demonstrable pathology in the urinary tract or adjacent viscera, namely: (a) curvature of the lumbar spine with convexity away from the diseased side with consequent narrowing of the costo-iliac space on the affected side, and (b) clouding or obliteration of the psoas muscle shadow.

Instructive cases have been recorded by a number of writers emphasizing the fact that disease in structures adjacent to the kidney area can simulate perinephritic abscess. Kessler, Bennetts, and Bacon (1) stress the frequency of adjacent bone lesions. Rusche and Bacon (2) reported ten cases illustrating extraneous lesions explored for suspected perinephric abscess. Wever and Perry (3) reported a case of fatal perirenal hemorrhage from periarteritis nodosa with classical signs and symptoms of perinephritic abscess. Brown (4) reported a case of traumatic myositis as a cause of paranephric abscess.

The roentgenographic evidence of perinephritic abscess, emphasized by Beer (5), Lipsett (6), and others, proved very helpful. The results in both cases illustrate the value of prompt surgical exploration in suspected perinephritic abscess. Negative findings in the perirenal space led to the suspicion of a pararenal lesion and further exploration revealed the true pathological condition in the exposed psoas muscle.

Furunculosis was undoubtedly the source of the infection in the first case. The same type of organism was recovered in culture from the pus in the abscess and the skin lesion. Because of the prompt healing of the wound and the absence of residual symptoms, it is not unreasonable to assume that the muscle abscess was a primary metastatic lesion. In the second case, palpation of bare bone is suggestive of an early osteomyelitis of the vertebra with secondary abscess in the muscle. The negative spine X-ray examinations in both cases do not necessarily exclude osteomyelitis. It is positive only in the presence of advanced bone destruction.

SUMMARY

1. Lesions in structures adjacent to the kidney area not infrequently produce symptoms and signs identical with perinephritic abscess.

2. A diagnosis of perinephritic abscess warrants prompt surgical exploration.

3. Negative findings in the perirenal space should lead to the suspicion of disease in an adjacent structure.

4. Two cases of suspected perinephritic abscess proved to be psoas muscle abscess at operation.

5. Incision and drainage resulted in a prompt recovery.

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PUBERTAS PRAECOX: A SURVEY OF THE REPORTED CASES AND VERIFIED ANATOMICAL FINDINGS*

With Particular Reference to Tumors of the Pineal Body

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It is the general impression and the oft repeated statement that tumors of the pineal body are commonly associated with, and possibly responsible for, the premature development of sex characters—a condition commonly designated as pubertas praecox. In the male this condition manifests itself in the form of macrosomia genitalis, in the premature appearance of an excessive growth of hair, particularly in the pubic, axillary and facial regions, and in the increase in libido, shown in early masturbation. In the female it expresses itself in the early appearance of the menstrual cycle, in the prominence of the breasts and other manifestations of premature development of sex characters. This notion was in the main based upon the reported instances of verified tumors of the pineal body which were found to be associated, mainly in the male, with what was considered to be an excessive and premature development of sex characters. Bailey and Jelliffe (1), however, in their classic review of the recorded pineal tumors, raise the question whether the precocious sex development, when occurring in association with a pineal tumor, is not due to a disturbance caused by this tumor elsewhere in the brain. They have drawn attention to the obscurity of the physiology of the pineal body in man and have pointed out that it loses its glandular structure very early in its postnatal life. Hence they concluded that, whatever its function, it is confined to childhood. Earlier and more recent experiments have failed to define accurately and substantially the significance of this organ. Feeding of the pineal body substance, implantation or the removal of this organ and injections of its extracts were employed in several species of experimental animals for the purpose of establishing or excluding the presumptive influence of this structure as a regulator of the development of sex characters, with varying, and hence, inconclusive, results.

Feeding of the substance of fresh pineal "glands" to over four hundred young animals (chickens, guinea-pigs and dogs) was reported by McCord (2) to have resulted in early precocity and adiposity. Hoskins (3), on the other hand, in similar animal experiments obtained almost entirely negative results.

Kozelka (4) reported negative results from implantation of the pineal body into the chick, while Dubowik (5) observed an increase in the rate of growth of the rabbit. Lahr (6), working with rats, found only a retardation of gonadal development in both the female and male without any influence on the body growth in either sex.

Pinealectomy gave consistently negative results, as reported by Foa (7) in the rat; by Exner and Boese (8) in the rabbit; by Dandy (9) in the dog; and by Badertscher (10) in the chick. However, positive results in the rat were reported by Izawa (11); by Horrax (12) in the guinea-pig; by Clemente (13) in the rabbit; by Shartischi (14) in the dog; and by Foa, Clemente and Zoia (15) in the chick.

Extracts of the pineal body were injected into the experimental animal by Von Cyon (16), Exner and Boese (17), Fenger (18), and Dana (19), all of whom reported negative results. Similar experiments carried out by Jordan (20) and Dixon and Halliburton (21) produced lowering of blood pressure, while Engel (22) noted an antagonistic effect on the growth hormone of the anterior lobe of the hypophysis and the hormone operative in the luteinization and maturation of the follicles. Of greater significance, however, are the results obtained by Rowntree (23) and his co-workers. In their well controlled experiments with injections of the pineal extract they have noted an accelerated rate of differentiation resulting in hastened adolescence of the animal with dwarfism developing alongside relative macrogenitalism. This is perhaps the strongest evidence favoring the view that the pineal body is a gland of internal secretion, and, as such, is active as a regulator of the development of sex characters at one time or another in the life of the animal. However, some doubt is thrown upon the probable glandular structure and the endocrine function of the pineal body by investigators who, having studied a number of pineal tumors, reached the conclusion that in its fully developed or neoplastic state the pineal body is not a gland and hence can play no part as an endocrine organ in the development of sex characters. On the other hand, Tilney and Warren (24), studying the pineal body from a phylogenetic point of view, have come to the conclusion that this structure at some stage of its phylogeny and embryogenesis had retained for a period of time the structure of a glandular organ. This view has found some support in the observations of Globus and Silbert (25), who, in their study of the normal human pineal body, have traced it through various stages of development from an early embryonal phase to maturity and found that in its early foetal stage it has a structure which is glandular in character (fig. 1). They also found that it retains this glandular character only for a limited length of time, and acquires a new organization characterized by a mosaic grouping of two cell forms (fig. 2), which again is transient and retained only during the first few months of postnatal life. From then on the pineal body slowly acquires the structure characteristic
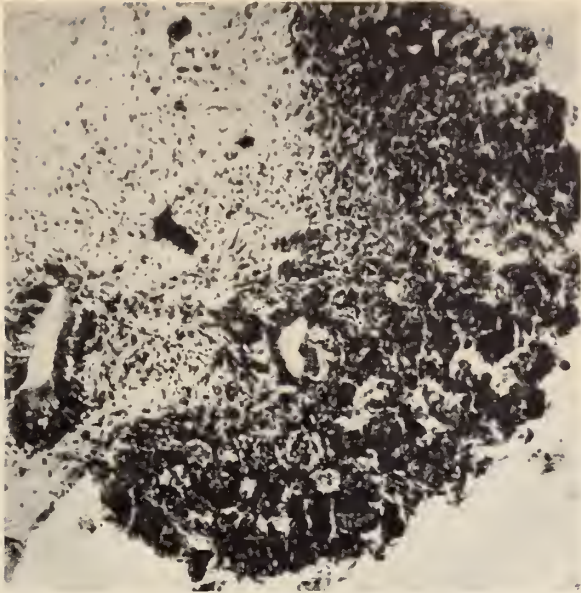
FIG. 1. Pineal body in a foetus at $5\frac{1}{2}$ months ($\times$ 50)
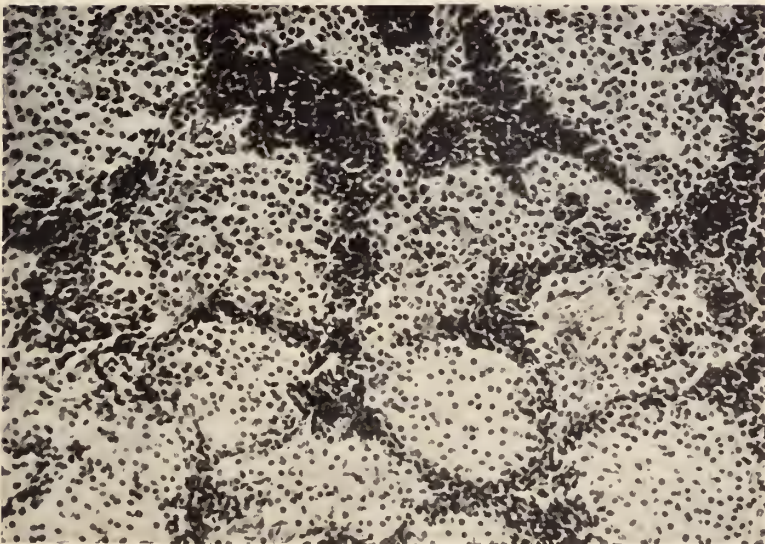
FIG. 2. Section of pineal body of an infant, 28 days old, showing typical mosaic arrangement of the two distinct types of cells ($\times$ 260)

of its mature state (fig. 3). This would seem to suggest the possibility that the pineal body functions as a gland through a limited period of time during the foetal life of the organism. At such time it asserts its

influence upon the evolution of the sex characters and lays the foundation for their future development. Then, with a change in the structure, it loses its functions as a gland, delegating such activities to some other endocrine organ.

Thus it is obvious that no definite conclusions as to the form and function of the pineal body have, as yet, been agreed upon, nor can they be reached on the basis of the controversial morphologic and experimental observations made so far. Hence, it seemed to us advisable to review more carefully the clinical observations recorded in the literature on the subject of pubertas praecox and to re-examine the data presented concerning the etiologic factors of this symptom complex. Accordingly, we
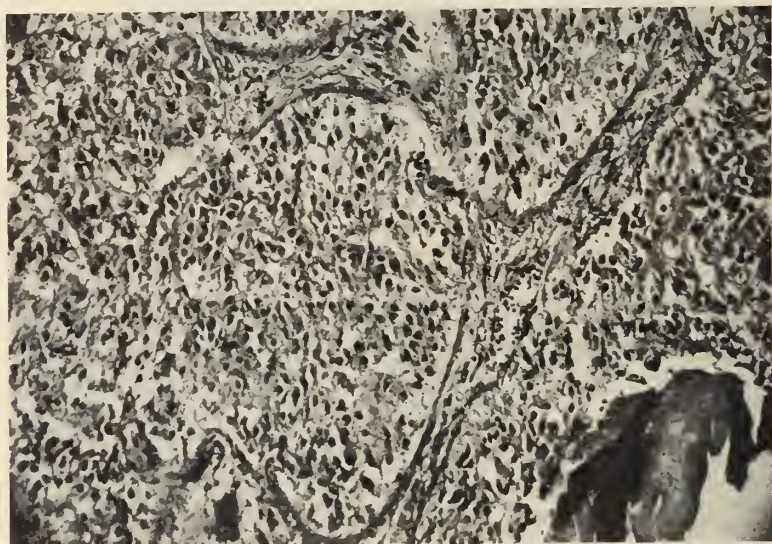
FIG. 3. Section of pineal body of man, aged 42 years ($\times$ 270)

have surveyed all of the reported instances of tumors of the pineal body; recorded cases of premature development of sex characters in which tumors were disclosed in parts of the brain neighboring upon the pineal region; instances in which pubertas praecox had been associated with tumors of the gonads or adrenal glands; and, finally, such cases in which the syndrome of pubertas praecox was described only clinically, there being no available surgical or post mortem findings.

In analyzing the results of this survey, we have kept before us the following questions:

   1. Do primary tumors of the pineal body have a direct influence over the development of sex characters?
   2. Do tumors in the pineal body indirectly contribute toward the

disturbances in the development of the sex characters by causing alterations in an adjacent part of the brain, such as the *diencephalon*?

3. Do manifestations such as polyuria, polydipsia, adiposity, somnolence, non-febrile alterations in temperature and pulse rate and other allied disturbances, frequently considered as deviations in the vegetative functions, occur side by side with alterations in sex character development; and, if so, can they all be due to a lesion affecting some part of the diencephalon, the presumptive seat of a vegetative center?

4. What interpretation can be placed on the occurrence of disturbances of vegetative function, coincident with the presence of a pineal tumor, in the absence of pubertas praecox? And, finally,

5. Are there disease processes elsewhere in the human body which may be regarded as the more likely cause for the alterations or deviations in the sex character development?

The answer to the first question may, in part, be found in an analysis of the clinical manifestations and anatomical findings disclosed in 177 cases of tumors of the pineal body, collected from the literature. Of these, 113 were already fully reviewed by Haldeman (26), who searched through the literature covering a period of 125 years, from 1800 to 1925. During the subsequent twelve years (until 1937), seventy-three added cases were reported, as listed in the accompanying chart (table 1). It is rather significant that of the entire number of 177 cases of pineal tumors only twenty-one cases were described as presenting features of pubertas praecox. In an attempt to evaluate the significance of this rather small ratio, it is essential to bear in mind that, among the 177 cases, 107 were of an age which exceeded that of fifteen years, while in thirteen instances no age was recorded. It is obvious that in only fifty-six cases which fell into what appears to be an arbitrarily selected age group, fifteen years or below, could the symptom complex of pubertas praecox be accepted as of diagnostic significance. Thus, of course, the fact that twenty-one cases out of fifty-six (37.5 per cent) displayed the symptom complex, assumes greater importance and would seem to favor the view that the pineal body has some influence in the production of the syndrome. At least, it cannot be ignored unless other observations may put a new interpretation on these data. Such is the case when it is realized that precocious sex character development, when found in association with verified pineal body tumors, has been noted almost exclusively in the male. It raises the question as to whether it is possible for a central organ, such as the pineal body, to exercise its supposed endocrine function, in a manner to affect only the male of the species. This, being rather unlikely for a structure which has an identical form and location in both sexes, throws further doubt on the endocrine character of the organ impugned.

In considering the second question, it should be noted, as shown in

TABLE 1

SERIAL NUMBER	AUTHOR	YEAR	BIBLIOGRAPHY NUMBER	SEX	AGE	TYPE OF TUMOR
114	Meyer	1918	29	M.	11	Teratoma
115	Martin	1923	30	M.	23	Neuroglioma
116	Martin	1923	30	F.	13	?
117	Bienstock	1926	31	M.	23	Sarcoma
118	Kutschevenko	1926	32	M.	17	Adenoma
119	Stark	1927	33	M.	25	Pinealoma
120	Haldeman	1927	34	M.	49	Glioma
121	Horrax	1927	35	M.	40	Pinealoma
122	Davidson	1927	36	M.	32	Tumor
123	Horrax and Bailey	1928	37	M.	40	Ganglioneuroma
124	Horrax and Bailey	1928	37	M.	9	Pinealoma
125	Hückel	1928	38	M.	31	Sarcoma
126	Rosenfeld	1929	39	M.	10	Pinealoma
127	Derman and Kopelowitsch	1929	40	F.	27	Neuroglioma
128	Glaser	1929	41	F.	6	Pinealoma
129	Mankowsky and Smirnow	1929	42	M.	22	Pinealoblastoma
130	Schmincke	1929	43	M.	50	Ganglioneuroma
131	Altmann	1930	44	M.	11	Dermoid cyst
132	Dias	1930	45	M.	8	Pinealoma
133	Handley	1930	46	F.	42	Cyst
134	Handley	1930	46	F.	42	Cyst
135	Arend and Schusterowna	1930	47	M.	10	Pinealoma
136	Wirth	1930	48	M.	$6\frac{3}{4}$	Chorioepithelioma
137	Globus and Silbert	1931	49	M.	13	Pinealoma
138	Globus and Silbert	1931	49	M.	17	Pinealoma
139	Globus and Silbert	1931	49	M.	13	Pinealoma
140	Globus and Silbert	1931	49	M.	30	Pinealoma
141	Globus and Silbert	1931	49	M.	37	Pinealoma
142	Globus and Silbert	1931	49	M.	20*	Pinealoma
143	Globus and Silbert	1931	49	F.	11	Pinealoma
144	Van Wagenen	1931	50	F.	34	Spongioblastoma
145	Kux	1931	51	M.	22	Pinealoma
146	Straub	1931	52	M.	19	Pinealoma
147	Jaensch	1931	53	M.	35	Tumor
148	Globus	1932	54	M.	$2\frac{1}{2}$	Pinealoma
149	Globus	1932	54	F.	11	Pinealoma
150	Gautier, Jentzer and de Morsier	1932	55	F.	9	Pinealoma
151	Allen and Lovell	1932	56	M.	19	Teratoma
152	Allen and Lovell	1932	56	M.	15	Spongioblastoma
153	Harris and Cairns	1932	57	M.	20	Pinealoma
154	Baudouin, Lhermitte and Lereboullet	1932	58	M.	18	Pinealoma
155	Vincent and Rappaport	1933	59	M.	40	Pinealoma
156	Kubo	1933	60	M.	19	Pinealoma

* Months.

TABLE 1—*Concluded*

SERIAL NUMBER	AUTHOR	YEAR	BIBLIOGRAPHY NUMBER	SEX	AGE	TYPE OF TUMOR
157	Guillain, Mollaret and Bertrand	1933	61	M.	32	Pinealoma
158	Ragan	1934	62	M.	15	Pinealoma
159	Stringer	1934	63	M.	27	Spongioblastoma
160	Alajouanim, Thurel and Oberling	1934	64	M.	47	Neurospongioma
161	Friedmann and Scheinker	1934	65	M.	53	Neuroepithelioma
162	Ku	1935	66	M.	25	Cyst
163	Friedman and Plaut	1935	67	M.	33	Pinealoma
164	Zeitlin	1935	68	M.	14	Mixed tumor, teratoid features
165	Zeitlin	1935	68	M.	45	Astroblastoma
166	Zeitlin	1935	68	M.	21	Psammoma
167	David, Mahoudeau, Askenazy and Brun	1935	69	F.	27	Pinealoma
168	Schaeffer	1935	70	M.	39	Glioblastoma
169	McLean	1935	71	M.	6	Teratoma (parapineal)
170	Dandy	1936	72	M.	10	Teratoma
171	Dandy	1936	72	M.	15	Pinealoma
172	Dandy	1936	72	F.	28	Pinealoma
173	Horrax	1936	73	F.	42	Pinealoma
174	Horrax	1936	73	M.	10	Pinealoma
175	Schaeffer, de Martel and Guillaume	1936	74	M.	25	Astrocytoma
176	Groff	1937	75	M.	18	Pinealoma
177	Horrax	1937	76	M.	10	Pinealoma

another chart (table 2) that, among the twenty-one cases of pineal tumor with evidence of pubertas praecox, the tumor did not remain restricted in location nor in its effects, but caused morphologic alterations elsewhere in the brain either by extension into adjacent parts of the brain, such as the corpora quadrigemina (fig. 4), the thalamus (fig. 5), and the third ventricle (fig. 6), or by obstructing the aqueduct of Sylvius and blocking the cerebrospinal fluid drainage, causing internal hydrocephalus. The latter, in turn, often brings about alterations in the floor of the third ventricle (fig. 7), the tuber cinereum and other parts of the hypothalamus, a subdivision of the brain stem which has acquired a significant position in the physiology of vegetative functions. While it still cannot be definitely said that the symptoms of precocious development are due to pathologic changes in any one of the aforementioned parts of the diencephalon, it is, nevertheless, equally true that no longer can it be maintained with any degree of certainty that the pineal body alone is responsible for the production of the syndrome.

TABLE 2

CASE NUMBER	AUTHOR	SERIAL NUMBER	AGE	SEX	ANATOMIC FINDINGS		DEVELOPMENTAL SEX CHARACTERISTICS	PHYSICAL DEVELOPMENT	PULSE, TEMPERATURE	SOMNOLENCE	INCONTINENCE	POLYPHAGIA; POLYDIPSIA; POLYURIA	REMARKS
					Pineal body	Brain							
1	Joukousky	48	6 days	F.	Cystic tumor Hyperplastic (size of a big almond).	Absence of hemispheres, corpus callosum and fornix. Aqueduct of Sylvius obliterated. Anterior part of corpora quadrigemina flattened. Internal hydrocephalus.			Bradycardia. Subnormal temperature.	Present.			Pituitary gland normal.
2	Globus	148	2½	M.	Pinealoma with supratentorial extension.	Disorganization of the midbrain. Third ventricle dilated. Major portion of tumor found in left lateral ventricle.			Elevated.				
3	Brosa	102	3	M.	Sarcoma.	Internal hydrocephalus.				Present.			
4	Horrax, Bailey	107	3	M.	Cystic teratoma.	Dilatation of the ventricles.	Enlarged genitalia.	Much taller than normal (41.5 inches). Obesity.					
5	Holzhauer	49	4	M.	Cystic.	Replaced posterior part of third ventricle, extending into cerebral peduncles. Internal hydrocephalus.	Enlarged genitalia.	Taller than normal.	Bradycardia. Irregularity.	Very quiet.			
6	Oestreich, Slawyk	43	4	M.	Psammo-sarcoma.	Internal hydrocephalus. Infundibulum dilated. Cerebral peduncles flattened. Third ventricle occupied by tumor.	Enlarged genitalia. Secretion from breasts. Pubic hair present.	Taller than normal (108 cm.) Obesity.	Bradycardia. Irregularity.			Polyphagia. Polydipsia.	

7	Frankl, Hochwart	56	5½	M.	Teratoma.	Internal hydrocephalus. Aqueduct of Sylvius dilated by compression. Corpora quadrigemina pushed laterally and caudally. Microscopic infiltration of the brain tissue.	Enlarged genitalia. Erections. Adult voice. Pubic hair present.	Taller than normal (123 cm).		Present.
8	Luce	96	5½	F.	Teratoma.	Corpora quadrigemina were covered. Internal hydrocephalus.		Obesity.	Moderate tachycardia.	
9	Ogle	42	6	M.	Teratoma.	Replaced the third ventricle. Thalami pushed away. Corpora quadrigemina flattened. Internal hydrocephalus.	Enlarged genitalia. Pubic hair present.			Present.
10	Horrax, Bailey	105	6	M.	Spongioblastoma.	Splenium of corpus callosum flattened. Third and fourth ventricles replaced. Internal hydrocephalus.		Taller than normal (129 cm.). Exceptionally well-developed.		
11	Glaser	128	6	F.	Pinealoma (3.5 x 2 x 1 cm.)	Internal hydrocephalus. Tumor extended into third ventricle.		Very well developed.		Present.
12	Wirth	136	6¾	M.	Atypical chorioepithelioma.	All ventricles dilated. Mass occupied region of pineal gland and quadrigeminal plate, also lingula and anterior medullary velum. Anterior portion of cerebellum compressed, aqueduct of Sylvius not found. Roof of skull thin, with prominent markings. Dura under tension.	Markedly enlarged genitalia Pubic hair present.		Tachycardia.	

TABLE 2—*Continued*

CASE NUMBER	AUTHOR	SERIAL NUMBER	AGE	SEX	ANATOMIC FINDINGS		DEVELOPMENTAL SEX CHARACTERISTICS	PHYSICAL DEVELOPMENT	PULSE, TEMPERATURE	SOMNOLENCE	INCONTINENCE	POLYPHAGIA; POLYDIPSIA; POLYURIA	REMARKS
					Pineal body	Brain							
13	Steiner, Tohan	99	7	M.	Highly cellular tumor, probably of the pineal body. Adenoma.	Tumor of tectum of mid-brain. Lamina quadrigemina destroyed. Tumor replaced posterior part of thalami and of third ventricle. Internal hydrocephalus.	Enlarged genitalia. Pubic and axillary hair present. Hair on upper lip and chin present.	Developed to equivalent of 10–12 year old boy.	Bradycardia.		Urinary.		
14	Gutzeit	32	7¾	M.	Teratoma.	Internal hydrocephalus. Tumor extended into third ventricle, pushing thalami aside and replacing the region of the corpora quadrigemina.	Pubic hair present.	Well developed.	Bradycardia.	Marked.	Urinary and fecal.	Polyphagia.	
15	Boehm	84	9	M.	Teratoma.	Internal hydrocephalus. Tumor invaded and dilated third ventricle and extended to chiasma. Basal ganglia compressed. Hemorrhages present in surrounding brain.	Adult genitalia. Pubic and axillary hair present. Adult voice.	Exceptionally well-developed.	Tachycardia. Slightly elevated temperature.				
16	Marburg	54	9	F.	Mixed tumor (pineal tissue, choroid plexus, and glia).	Internal hydrocephalus. Left pulvinar compressed. Tumor extended into anterior corpora quadrigemina.		Obesity.					
17	Hijmans, van den Bergh, van Hasselt	67	9	M.	Teratoma.		Enlarged genitalia. Pubic hair present.						

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No.	Author		Age	Sex	Tumor	Pathological anatomy	Sexual development	General development	Temperature	Diabetes	Pituitary
18	Horrax, Bailey	124	9	M.	Pinealoma. Teratoma (?).	Internal hydrocephalus. Tumor extended from splenium of corpus callosum to calamus scriptorius. Cerebellum pushed upward and backward.	Markedly enlarged genitalia. Spermatogenesis present.			Diabetes insipidus noted(?).	
19	von Hoesslin	33	9	M.	Spindle-cell sarcoma.	Tumor adherent to cerebellum. Corpora quadrigemina flattened and not distinguishable. Aqueduct of Sylvius closed. Floor of fourth ventricle sclerosed. Internal hydrocephalus.				Diabetes insipidus.	
20	Gautier, Jentzer, de Morsier	148	9	F.	Pinealoma.	Third ventricle filled with tumor mass. Optic chiasm and infundibulum infiltrated. Internal hydrocephalus.	Pubic, axillary and facial hair present.		Slight nocturnal elevation of temperature.	Polydipsia. Polyuria.	Stalk and body of pituitary enlarged, but not involved in tumor Sella turcica normal.
21	Skoog	83	9	M.	Pineal tumor (compressed pineal gland (6.2 x 4.8 cm.) (14.5 gr.).		Enlarged genitalia. Spermatogenesis and erections present.	Very well developed. Obesity, followed by emaciation.			
22	Odermalt	75	10	M.	Teratoma (3 x 2.4 x 2.7 cm.).		Erections present. Voice changes present. Pubic hair present.	Prematurely developed.			

TABLE 2—Continued

CASE NUMBER	AUTHOR	SERIAL NUMBER	AGE	SEX	ANATOMIC FINDINGS Pineal body	ANATOMIC FINDINGS Brain	DEVELOPMENTAL SEX CHARACTERISTICS	PHYSICAL DEVELOPMENT	PULSE, TEMPERATURE	SOMNOLENCE	INCONTINENCE	POLYPHAGIA; POLYDIPSIA; POLYURIA	REMARKS
23	Horrax	172	10	M.	Pinealoma.	Operation performed, no autopsy. Tumor bulged into posterior part of third ventricle and into greatly dilated lateral ventricles. Tumor projected beneath the tentorium and compressed cerebellum.	Genitalia and voice of adult type. Pubic, axillary and facial hair of adult type.	Prematurely developed. Very muscular.					
24	Raymond, Claude	58	10	M.	Glioma (4 cm. in diameter).	Marked internal hydrocephalus. Third ventricle dilated. Corpora quadrigemina not recognized. Pons also involved.		Equivalent to that of thirteen year old boy. Marked obesity.					(Adenomatous formation found in adrenal cortex.)
25	Dandy	170	10	M.	(1) Teratoma (3 mgr.). (2) Recurrent teratoma (6.99 mgr.).	Recurrent teratoma noted two years later. Two operations performed.			Bradycardia.	Present.			
26	Takeya	70	10	M.	Teratoma.		Present, but no special details given.						
27	Altmann	131	11	M.	Dermoid cyst (4.5 x 5 x 5.5 cm.)	Internal hydrocephalus. Tumor extended into surrounding brain, invading third ventricle.		Obesity.					

No.	Author											
28	Globus	149	11	F.	Pinealoma.	Internal hydrocephalus. Tumor displaced tectum of mesencephalon and invaded right lateral ventricle.				Bradycardia. Periodic moderate elevations of temperature.		
29	Meyer	114	11	M.	Teratoma (4 cm. in diameter).	Internal hydrocephalus. Tumor invaded third ventricle and part of cerebellum. Fourth ventricle also replaced.	Pubic and axillary hair present.					
30	Frank, Huebschmann	86	11½	M.	Small cell epithelial tumor. Teratoma (?).	Internal hydrocephalus. Tumor adherent to midbrain.	Testes well developed. Spermatogenesis present. Voice matured. Pubic hair present.	Very well developed. Taller than normal (162 cm.). Larynx size of an adult.				Polydipsia.
31	Bailey, Jelliffe	63	12	M.	Teratoma (3.75 cm. in diameter).	All ventricles enormously dilated. Aqueduct of Sylvius obliterated. Corpora quadrigemina flattened.		Well developed. Obesity.		Present.	Urinary and fecal.	
32	Ganderer	27	12	M.	Teratoma (3.5 x 2.5 cm.).	Internal hydrocephalus. Corpora quadrigemina destroyed. Tumor invaded third ventricle and compressed thalami.		Very well nourished.	Bradycardia. Irregularity.	Present.		

TABLE 2—Continued

CASE NUMBER	AUTHOR	SERIAL NUMBER	AGE	SEX	ANATOMIC FINDINGS Pineal body	ANATOMIC FINDINGS Brain	DEVELOPMENTAL SEX CHARACTERISTICS	PHYSICAL DEVELOPMENT	PULSE, TEMPERATURE	SOMNOLENCE	INCONTINENCE	POLYPHAGIA; POLYDIPSIA; POLYURIA	REMARKS
33	Horrax	78	12	M.	Stroma of pineal gland.	Internal hydrocephalus. Tumor seen in posterior half of lateral ventricle in region between tail of corpus callosum and medulla. In floor of greatly dilated third ventricle, tumor (2.2 cm.) not connected to primary tumor was found.	Genitalia very well developed. Voice mature. Pubic, axillary and facial hair very well developed.	Very athletic type. Taller than normal (160 cm.). Long bones large, especially at lower ends.		Present.		Polyuria.	
34	Lereboullet, Brizard	95	12	M.	Neuro-epithelial glioma (size of lemon).	Internal hydrocephalus. Aqueduct of Sylvius compressed. Third ventricle pushed aside. Pituitary gland compressed.	Genitalia very well developed. Voice mature. Pubic, axillary and facial hair well developed.	Resembled a well-developed dwarf. Considerable cachexia.		Present.	Urinary and fecal.		
35	Globus, Silbert	137	13	M.	Pinealoma (2.5 cm. in diameter).	Internal hydrocephalus. Lateral and third ventricles dilated. Tumor invaded pulvinar and rested on quadrigeminal plate.	Genitalia enlarged. Pubic hair sparse. Facial hair very well developed.		Slight bradycardia. Slight elevations of temperature.				
36	Zeitlin	162	14	M.	Mixed tumor (teratoid)	Internal hydrocephalus. Aqueduct of Sylvius occluded. Tumor extended to posterior part of third ventricle. Quadrigeminal plate compressed.	Genitalia underdeveloped.		Bradycardia. Elevation of temperature up to 103°.	Present.			

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37	de Mouchy	101	14	M.	Teratoma (malignant adenoma).	Internal hydrocephalus. Part of tumor situated between folds of dura mater, where falx and tentorium cerebelli meet.			Occasional elevations.	Present.	
38	Klapproth	94	15	M.	Teratoma (4.4 x 2.8 x 3.6 cm.).	Internal hydrocephalus. "Large, infiltrating."	Spermatogenesis less than normal.	Infantile.		Present.	Small adenoma of pituitary gland. Enlargement of thyroid gland (colloid).
39	Allen, Lovell	152	15	M.	Spongioblastoma.	Internal hydrocephalus. Tumor extended into dilated third ventricle and involved posterior and descending horns of right lateral ventricle. Corpora quadrigemina destroyed.		Poorly nourished.		Present.	
40	Ragan	158	15	M.	Pinealoma (5 x 3 x 3 cm.).	Tumor involved posterior portion of third ventricle. Aqueduct of Sylvius patent.		Large and well-developed.	Bradycardia.	Present.	
41	Dandy	171	15	M.	Pinealoma (4 mgr.).	Third ventricle dilated. Tumor attached to roof of third ventricle and quadrigeminal plate. (Seen at operation.)				Present.	
42	Goldzieher	65	16	M.	Angiosarcoma (3.5 x 3 x 3.5 cm.).	Internal hydrocephalus. Thalami compressed. Anterior quadrigemina destroyed. Remnant of posterior quadrigemina preserved. Aqueduct of Sylvius invaded. Third ventricle involved.	Genitalia adult. Pubic, axillary and facial hair very well developed.		Slight elevation of temperature.		Hyperplasia of adrenals. Pituitary small, microscopically normal. Metastases in lungs.

TABLE 2—Continued

CASE NUMBER	SERIAL NUMBER	AUTHOR	AGE	SEX	ANATOMIC FINDINGS — Pineal body	ANATOMIC FINDINGS — Brain	DEVELOPMENTAL SEX CHARACTERISTICS	PHYSICAL DEVELOPMENT	PULSE, TEMPERATURE	SOMNOLENCE	INCONTINENCE	POLYPHAGIA; POLYDIPSIA; POLYURIA	REMARKS
43	110	Horrax, Bailey	17	M.	Pinealoma (small).	Small tumor of pineal gland. Large vascular glioma (?) of third ventricle.						Polyuria.	
44	138	Globus, Silbert	17	M.	Pinealoma (2 x 2 x 3 cm.).	Midbrain destroyed. Aqueduct of Sylvius large. Tuber cinereum thin. Ventricles distended. Tumor occupied quadrigeminal plate.		Much taller than normal.				Polydipsia. Polyuria.	In hospital water intake and output normal.
45	174	Graff	18	M.	Pinealoma.	Lateral and third ventricles dilated. Pulvinar and thalamus invaded. Tuber cinereum, hypothalamus and pre-chiasmal region invaded.	Female distribution of hair.			Hypersomnia.		Polydipsia. Polyuria.	Visual fields showed irregular defects. Extraocular movements impaired.
46	20	Feilchenfeld	18	M.	Sarcomatous pineal tumor (size of "five dollar gold piece").	Internal hydrocephalus. Anterior part of corpora quadrigemina involved.			Gradual elevation of temperature.	Present.	Urinary and fecal.		
47	154	Baudouin, Lhermitte, Lereboullet	18	M.	Pinealoma.	Third ventricle dilated. Neoplastic transplant in ventral wall of third ventricle. Infundibulum compressed. Tuberous structures.		Emaciation.	Subnormal temperature.				Pituitary gland normal. Sudden loss of consciousness. Constipation.

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48	Reinhold	23	19	M.	Cystic tumor (size of hazel nut)	Internal hydrocephalus. Midbrain and pons flattened. Corpora quadrigemina pushed away. Left middle cerebral peduncle compressed.						Polyuria.	
49	Massot	8	19	M.	Carcinoma (3.3 x 3 x 2.8 cm.).	Internal hydrocephalus. Tumor in front of corpora quadrigemina. Tumor replaced third ventricle.						Polydipsia. Polyuria.	
50	Allen, Lovell	151	19	M.	Teratoma (size of walnut).	Brain extremely soft. Corpora quadrigemina degenerated. Internal hydrocephalus.				Intermittent.			
51	Horrax, Bailey	111	20	M.	Pinealoma.	Third ventricle dilated. Corpora quadrigemina compressed.	Genitalia underdeveloped. Female distribution of hair.					Polydipsia. Polyuria.	
52	Howell	60	22	M.	Gliosarcoma (?) (size of walnut).	Internal hydrocephalus. Third ventricle dilated. Aqueduct of Sylvius dilated. Tumor invaded roof and fourth ventricle.						Polydipsia.	
53	Daly	25	23	M.	Alveolar carcinoma (5.7 x 7.25 x 1.27 cm.).	Internal hydrocephalus. Tumor pressed upon corpora quadrigemina, which were soft and flattened.					Urinary and fecal.	Polyphagia (extreme).	
54	Lowenthal	87	23	M.	Malignant adenoma (2.3 x 2.9 cm.).	Internal hydrocephalus. Tumor occupied optic thalamus and extended into cerebral peduncles. Pons markedly flattened. Sella turcica excavated.	Testes (normal) adult.	Obesity.	Bradycardia.				Pituitary gland microscopically normal.

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TABLE 2—*Continued*

CASE NUMBER	AUTHOR	SERIAL NUMBER	AGE	SEX	ANATOMIC FINDINGS Pineal body	ANATOMIC FINDINGS Brain	DEVELOPMENTAL SEX CHARACTERISTICS	PHYSICAL DEVELOPMENT	PULSE, TEMPERATURE	SOMNOLENCE	INCONTINENCE	POLYPHAGIA; POLYDIPSIA; POLYURIA	REMARKS
55	Gowers	17	24	M.	Sarcoma.	Tumor between optic thalamus, posteriorly in front of corpora quadrigemina, which were destroyed (particularly the left). Tumor extended into aqueduct of Sylvius.		Marked emaciation.	Bradycardia. Irregularity. Slight elevation of temperatue.		Urinary.		
56	Hempel	45	24	M.	Carcinoma (size of hen's egg).	Internal hydrocephalus. Tumor pressed on veins of Galen. Tumor pressed into third ventricle, also into substance of optic thalamus. Corpora quadrigemina destroyed. Geniculate bodies pushed aside.							
57	Kup	162	25	M.	Cystic (histologically glia fibres and cystic changes).			Resembled man of 40–45 years. Hair gray at 18 years. Face wrinkled at 18 years. Arteriosclerotic changes.					Glands of internal secretion microscopically normal.
58	Stark	119	25	M.	Pinealoma (?).	Tumor invaded infundibulum and floor of third ventricle. Internal hydrocephalus.	Impotence.	Most of body hair completely disappeared.	Tachycardia.			Polydipsia. Polyuria.	Pituitary gland normal.

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59	Harris, Cairns	153	26	M.	Pinealoma (size of walnut). Resembled an "alveolar sarcoma" of testes (2.8 x 2.3 x 2.2 cm.).	Internal hydrocephalus. Corpora quadrigemina impaired.	Testes normal.			Present.		X-ray of skull showed erosion of sella turcica
60	Derman, Hopelo-witsch	127	27	F.	Neuroglioma ependymale embryonale of pineal gland (2.75 x 2 x 2 cm.).	Internal hydrocephalus. Deformed sella turcica. Pituitary compressed and congested. Aqueduct of Sylvius compressed. On inside of optic thalamus impression of tumor noted.		Dystrophia adiposogenitalis.			Strangury.	Symptoms first noted during pregnancy. Exacerbation during and following pregnancy.
61	Stringer	159	27	M.	Spongioblastoma gangliocellulare (3 x 2.7 x 2.8 cm.).	Internal hydrocephalus. Third ventricle obliterated by tumor. Metastatic implant involved hypothalamus. Tumor nodule also involved supra optic tract.			Marked elevations of temperature.	Coma.	Polydipsia. Polyuria.	Pituitary histologically normal.
62	Rorschach	69	27	M.	Gliosarcoma gangliocellulare (3 x 2.7 x 2.7 cm.).	Internal hydrocephalus. Tumor obliterated third ventricle, covered aqueduct of Sylvius, spread out posterior parts of thalamus. Anterior quadrigeminal bodies flattened. Histologic changes in optic thalamus and brain stem.		Obesity.	Bradycardia.	Present.		
63	Kny	28	32	M.	Sarcoma (size of walnut).	Internal hydrocephalus. Corpora quadrigemina compressed. Vein of Galen dilated.		Obesity.			Urinary and fecal.	

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TABLE 2—*Concluded*

CASE NUMBER	AUTHOR	SERIAL NUMBER	AGE	SEX	ANATOMIC FINDINGS		DEVELOPMENTAL SEX CHARACTERISTICS	PHYSICAL DEVELOPMENT	PULSE, TEMPERATURE	SOMNOLENCE	INCONTINENCE	POLYPHAGIA; POLYDIPSIA; POLYURIA	REMARKS
					Pineal body	Brain							
64	Guillain, Mollaret, Bertrand	157	32	M.	Pinealoma (size of cherry).	Tumor occupied corpora quadrigemina. Third ventricle penetrated. Thalamic nuclei destroyed.				Present.			
65	Friedman, Plant	163	33	M.	Pinealoma (no gross tumor in region of pineal body).	Cranial nerves infiltrated. Flat tumor masses on inside of dura mater. Continuous infiltration of spinal meninges. Nuclear inclusions throughout metastases. Small portion of anterior pituitary invaded by tumor. Masses of tumor tissue in choroid plexus of third ventricle. Fourth ventricle densely infiltrated. Changes of posterior pituitary noted.	Genitalia underdeveloped. Impotence. Female distribution of pubic hair.	Obesity of pituitary type.				Polydipsia. Polyuria.	
66	Berblinger	85	35	M.	Spongioblastoma (5 x 3.5 x 3.5 cm.).	Tumor involved corpora quadrigemina. Aqueduct of Sylvius compressed. Tumor invaded third ventricle and pushed cerebellum posteriorly. Floor of midbrain excavated. Internal hydrocephalus.	Genitalia very well developed. Pubic and axillary hair very well developed.	Moderate obesity.					Adrenals large—histologically normal.

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67	Horrax	121	40	M.	Pinealoma (1.8 x 0.7 cm.).	Internal hydrocephalus. Aqueduct of Sylvius blocked. Third ventricle dilated. Corpora quadrigemina flattened.			Present.			
68	Zeitlin	165	45	M.	Astroblastoma (1.5 x 1.0 x 1.6 cm.).	Internal hydrocephalus. Aqueduct of Sylvius filled with tumor mass. Lamina quadrigemina showed tumor extensions. Lateral ventricles dilated.		Bradycardia. Slight elevations of temperature.	Present.			
69	Haldeman	120	49	M.	Glioma (3.7 x 1.7 x 3 cm.).	Third ventricle dilated. Aqueduct of Sylvius pressed. Cerebellum compressed. Hole in tuber cinereum.					Urinary and fecal.	X-ray of skull showed complete obliteration of outlines of sella. Pathologically, sella was enlarged. Posterior part completely absent.

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In turning to the third question, a further analysis of the material, as listed in table 2, reveals the fact that, in fifteen of the twenty-one cases, the manifestations of pubertas praecox were associated with various constellations of signs and symptoms of vegetative dysfunctions, such as polydipsia, polyuria, polyphagia, somnolence and obesity in varying degrees of intensity. Thus, of this relatively small group of cases, a little more than 71 per cent presented signs and symptoms indicative of vegeta-

Fig. 4. Pineal tumor invading the quadrigeminal plate and depressing the aqueduct of Sylvius.

tive dysfunction which occurred alongside features of pubertas praecox. These observations are significant when considered in the light of accumulating evidence favoring the probability that the hypothalamus is the seat of a mechanism regulating vegetative functions (Globus (27)). They are particularly noteworthy in view of the fact that such disturbances frequently occur alongside alterations in the tempo and the degree of the development of sex characters, and that anatomical disturbances

in and about the hypothalamic region are often discovered in cases of precocious sex character development. Thus it seems close at hand to
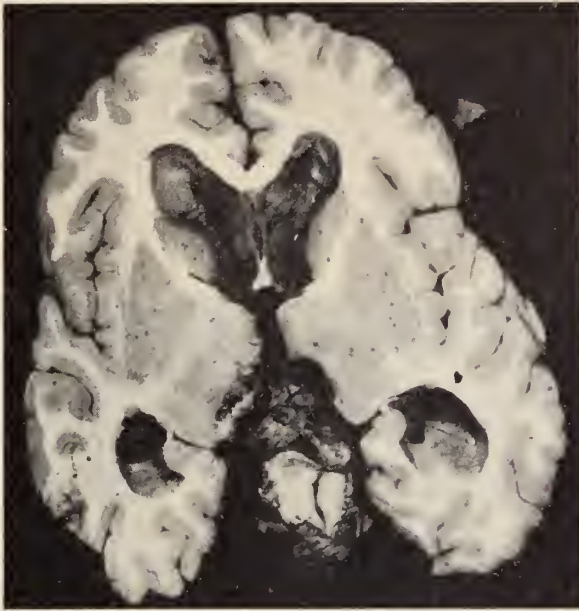
FIG. 5. Pineal tumor invading the posterior portions of the thalamus
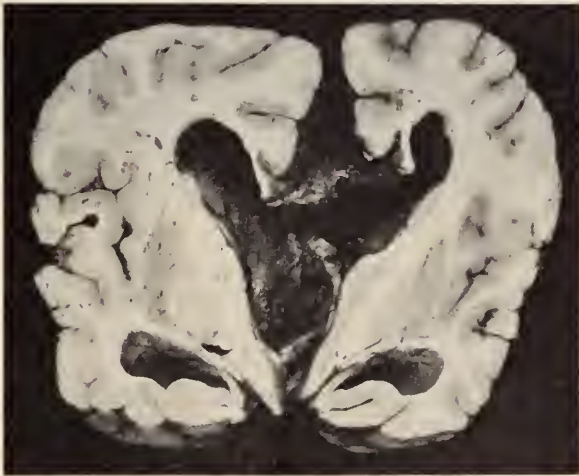
FIG. 6. Pineal tumor invading the third ventricle

assume that the hypothalamus, and not the pineal body, is the more probable seat of the disturbance causing this syndrome. This finds further support in the findings, as shown in table 2, that pineal tumors

often give rise to vegetative disturbances without alteration in sex charac-
ters, while, on the other hand, as shown in table 3, alterations in sex
character development may occur in instances in which the pineal body is
found uninvolved. Moreover, as noted in table 2, there are instances of
pubertas praecox in which, in addition to a pineal tumor, there is disclosed
at autopsy involvement of the adrenals, or the pituitary, or both.

At this point it is of interest to review the recorded cases of pubertas
praecox other than those associated with pineal tumors, in which there
was no evidence of disease of the pineal body. We were able to find in
the literature 544 of such cases. For convenience of analysis, we shall
divide them into two categories.
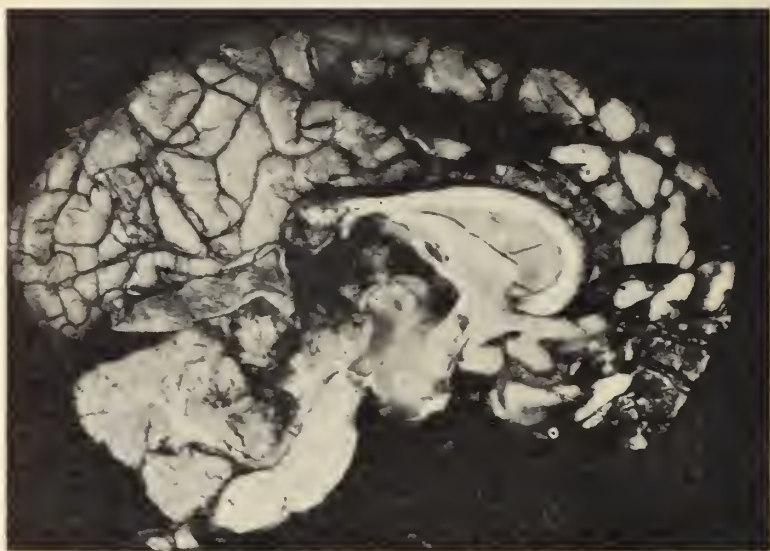
Fig. 7. Pineal tumor overlying the aqueduct of Sylvius causing marked hydro-
cephalus and extreme thinning of the hypothalamus

1. Cases in which autopsy or surgical findings were available. Of
these there were 104 cases, which are further subgrouped into: (a) forty-
four cases, thirty-three females and eleven males, which disclosed tumor of
the adrenal gland; (b) forty-two cases which revealed ovarian tumors;
(c) thirteen cases, twelve males and only one female, which showed
extensive disease of the brain; (d) four cases with testicular lesions; and
(e) one case with a lesion of the prostate. It is highly significant that
in this category there was such a high incidence of hyperplasia, or tumor
of the adrenal, or gonadal involvement, but the relatively high incidence of
brain affliction in this group also cannot be entirely ignored.

2. Cases in which clinical observations alone were available. This
category included 440, of which 334 cases were assembled by Reuben and

Manning (28), while the remaining 106 cases were found to have been reported in the literature since the time of publication of the above article. Among the female patients, of whom there were 338, there were twenty-eight instances in which there was a clinical history of an older or more recent involvement of the central nervous system. Among the males, of whom there were 102, twenty-three cases gave a similar history. This category, lacking precise anatomical information, is of little service in the study of the problem under discussion.

COMMENT AND CONCLUSION

From the data herein presented, it is obvious that, though the incidence of cases of pubertas praecox among verified cases of pineal tumors is not large, nevertheless it cannot be ignored. But it is also apparent that disturbances of other vegetative functions are quite frequently associated with verified pineal tumors. The latter occurrence finds a rational explanation in the fact that pineal tumors often extend rostrally beyond the limits of the midbrain into the diencephalic region, or, when restricted to the midbrain, frequently cause internal hydrocephalus, resulting in alterations in the hypothalamus, a part of the brain concerned with regulation of vegetative functions. This coexistence of vegetative disorders with disturbances of sex character development leads one to the consideration of the probability that the normal evolution of sex characters may be an expression of the vegetative organization of the body. With this in mind, it may be permissible to postulate the existence of a neural center in the domain of the hypothalamus, regulating with the aid of an endocrine organ, most probably the pituitary gland, the development of sex characters. This, in turn, leads to the thought that the precocious development of sex characters may be the result of some hypothalamic disorder, such as may be provoked by a tumor in the pineal region, particularly if the latter is teratoid in character and hence had its beginning early in the life of the individual.

However, there still remains the difficulty of explaining why, in the case of pineal tumors or hypothalamic lesions, it is the male sex that is predominantly affected, while in the female the precocious sex development is most often found to be associated with neoplasms or hyperplasia of either the gonads or the adrenal glands. This difficulty increases with the recognition of the fact that even in some of the males who displayed pubertas praecox the gonads or adrenals were the sites of the only verifiable disease process and that in some such cases there was present a pineal tumor associated with a neoplastic disease of the adrenal. This would seem to shift the weight of responsibility for this disorder to the gonads and adrenals, depriving the lesions in the central nervous system of the importance usually assigned to them. It also would seem to point to the more conservative conclusion that the manifestations of pubertas praecox

TABLE 3

CASE NUM-BER	AUTHOR	BIBLIOG-RAPHY NUM-BER	AGE	SEX	PATHOLOGY	REMARKS
1	Weissenberg	76	$3\frac{1}{2}$	M.	P.M.: Internal and external hydrocephalus. Other parts of brain normal. Pineal flattened, smaller than normal.	
2	Wieland	77	4	M.	Tumor of the third ventricle and of the falx.	
3	Schmid	78	$4\frac{1}{2}$	M.	Tumor involved third ventricle particularly its floor. It was connected to the infundibulum. Pituitary gland normal.	
4	le Marquand	79	4 yrs. 10 months	M.	Tumor on floor of third ventricle. "Hamartoma" tumor was small and occupied inter-peduncular space. Tumor was attached to right mamillary body and to tuber cinereum.	(1) B. P. 90/60. (2) Obesity. (3) Adrenal negative. (4) Hypothalamus and pituitary normal. (5) Pt. very intelligent.
5	Heuyer, Vogt	80	6	M.	Tumor in mammillary bodies compressing chiasm. Adrenals and testes normal.	(1) Headache. (2) Reflexes active, more so on left. (3) Mentally defective. (4) X-ray of skull showed calcified area in right hemi-sphere.
6	Dorff, Shapiro	81	$6\frac{1}{2}$	F.	Internal hydrocephalus. Atrophy of mammillary bodies. Chronic ependymitis. Sclerosis of basal leptomeninges. Corpus callosum thin. Sella flattened and broadened. Pituitary histologically normal.	(1) Hyperplasia of ovaries with microscopic degenera-tion. (2) Colloid goitre. (3) Miliary cortical adenomata of right adrenal gland.
7	Horrax, Bailey	82	7	M.	Internal hydrocephalus. Third ventricle involved. Infundibulum altered. Tumor of third ventricle: ganglioneuroma. Pineal flattened and elongated—histologically normal.	Marked obesity.

8	Vickers, Tioswell	83	8	M.	Tumor, size of walnut, involving floor of third ventricle. Tuber cinereum and mammillary bodies obliterated. Tumor pushed on basis sphenoid. Diagnosis: astrocytoma. Pituitary and adrenal normal.	(1) Premature ossification of bones. (2) Note: "No clinical evidence of cerebral tumor." (3) Fits and irritability since age of four. (4) At eight: 6-12 × daily—death.
9	Hellner	84	12	M.	P.M.: Diffuse inflammatory disease, particularly about hypothalamus. Many giant cells. Diagnosis: hypothalamic disease. Tuberculous encephalitis.	(1) At operation nothing found. (2) Diabetes insipidus, polyuria. (3) Bilateral papilledema. (4) Hypotonia.
10	Poos	85	12	M.	Generalized tuberculosis. No brain tumor. Ependymitis. Granular productive meningitis. Diagnosis: chronic tuberculous meningo-encephalitis.	(1) X-ray of skull negative. (2) Polyuria before death. (3) Bitemporal hemianopsia. (4) Lumbar tap: 54 cells, increased pressure.
11	Thomas, Schaeffer	86	12	M.	P.M.: Inflammatory lesion of tuber cinereum.	(1) Difficulty in walking. (2) Euphoria. (3) Internal hydrocephalus.
12	Schmalz	87	12	M.	P.M.: Third ventricle dilated. Brain and basal ganglia infiltrated. Caudate nucleus and part of internal capsule not infiltrated. Bulk of tumor on floor of third ventricle. Adrenal and pituitary normal.	Virile constitution.
13	Heilmann, Rückart	88	14	M.	P.M.: Mixed tumor of choroid plexus. Marked destruction in region of fornix, caudate nucleus, and mamillary bodies. Corpora quadrigemina flattened. Pineal: cholesteatoma, only a few tumor cells noted microscopically.	(1) Somnolence. (2) B. P. 90/50. (3) Hands red, feet cold. Drawing and tingling sensations. (4) Lacrimation. (5) Verbal expression of thoughts poor. (6) Marked hyperacusis. (7) Pt. resembled an adult.

TABLE 3—*Concluded*

CASE NUM-BER	AUTHOR	BIBLIOG-RAPHY NUM-BER	AGE	SEX	PATHOLOGY	REMARKS
14	Berblinger	89	16	M.	P.M.: Tumor occupied basal ganglia, extending to corpus callosum, floor of third ventricle, and to corpora quadrigemina. Tumor surrounded region of pineal. No trace of pineal. Diagnosis: glioblastic sarcoma.	Exceedingly marked cachexia.
15	Nothnagel	90	17	M.	P.M.: Internal hydrocephalus. Aqueduct of Sylvius compressed. Corpora quadrigemina spread apart. Diagnosis: Glioma of corpora quadrigemina.	(1) Polydipsia and polyuria. (2) Obesity. (3) Bradycardia. (4) Urinary and fecal incontinence. (5) Somnolence.
16	Luce	91	21	F.	P.M.: Tumor reached floor of third ventricle. Diagnosis: Angiosarcoma of base of brain. Pituitary normal.	(1) Hyperkeratosis of nails. (2) Obesity. (3) Blood sugar: 210 mgr.
17	Askanazy, Brack	92	22	F.	P.M.: Microcephalia. Microgyria. Hypoplastic pineal.	(1) Idiocy. (2) Secondary sex characteristics first noted at age of 10 yrs. (3) Mature at 11 yrs.

are most likely the result of an interplay between the functions of the endocrine organs, such as the adrenal glands and the gonads on the one hand, and the regulating activity of a hypothalamic center, probably mediated by the pituitary gland, on the other, with the pineal body adding at times its influence because of its anatomical position as a mechanical factor causing obstructive hydrocephalus with resulting disturbance in the hypothalamus.

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CARDIOVASCULAR LESIONS IN AVITAMINOSES

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In recent years attempts have been made to attribute certain cases of cardiac insufficiency of obscure nature to a subclinical avitaminosis (Weiss and Wilkins). It seems appropriate, therefore, to survey the established cardiovascular lesions in conditions of actual, discrete avitaminosis.

Alterations of the cardiovascular system associated with vitamin deficiency diseases have been observed by various authors at the autopsy table. Foremost among them are the beri-beri heart, the Moeller-Barlow heart, and the enlargement of the heart in rickets, which has been described by several pathologists. Experimental research in animals to determine the pathognomonic features of vitamin deficiencies have added interesting facts. In order to present the accumulated material in an intelligible way I shall take up each form of vitamin deficiency and present first the observations in man and then those in experimental animals.

Vitamin A deficiency has not been found to be associated with any significant alterations of the cardiovascular system, as far as I could ascertain.

Vitamin B deficiency presents well known clinical and pathological alterations in the heart, both in the adult and in the infant. A striking feature of beri-beri, outside of the nervous manifestations, is the severe cardiovascular symptom complex. The marked enlargement of the heart, the intense dyspnea, the rapid pulse, the cardiac sounds, the loud arterial pistol shot sound, and the frequent sudden collapse, so-called Shoshin, have for a long time been known to physicians in the far East. The latest classical description of the clinical and pathological features of the disease has been made by Wenckebach after special study in the Dutch East Indies. His monograph on the beri-beri heart has been freely consulted in the preparation of this paper. I am also under obligation to Professor Hu of the Medical College in Peiping and to Professor Ogata of the Imperial University in Tokyo, who were kind enough to send me material for histologic studies.

On macroscopic examination (Fig. 1) the heart is very flabby, easily torn, especially the right chamber. Both right ventricle and auricle are very much enlarged, due to dilatation. Particularly striking is the dilata-

tion of the conus arteriosus. Findings identical with those in adults are encountered in infants, chiefly in breast-fed babies of beri-beri mothers.

Histologic examination reveals a striking feature (Fig. 2), which was noted by the first authors who studied beri-beri. Thus, Dürck in 1905 states that the muscle fibres appear like hollow tubes, and speaks of sarcoplasmolysis. Mebius refers to identical changes as myodegeneratio hydropica. Wenckebach found the same striking vacuolization of the muscle fibres, which is not due to fatty infiltration. The muscle fibres are separated by conspicuous interfibrillar edema. The striking feature in the beri-beri heart is, according to him, a peculiar retention of water.
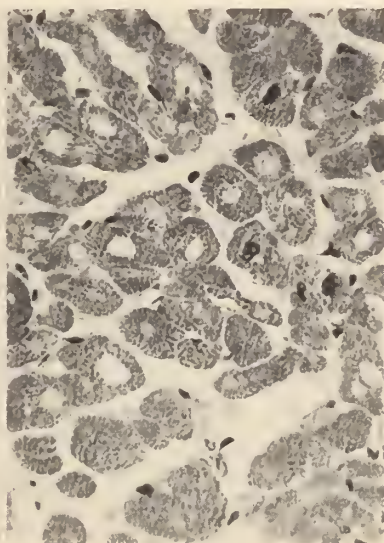
FIG. 1   FIG. 2

Wenckebach sees the chief factor of the pathologic physiology in a dilatation of the peripheral arterioles, which causes an increase in the venous pressure thus driving the blood with great force into the right ventricle. This accounts for the dilatation. The histopathology, however, remains unexplained. If one studies the figures in Wenckebach's and Dürck's articles one is impressed by the similarity of the peculiar vacuolization in beri-beri to that found in glycogenosis of the heart. Wenckebach and Dürck have not determined whether the vacuoles correspond to stored glycogen. My material was unfortunately not properly fixed and the result of glycogen stains is therefore not conclusive, although I found some glycogen within the muscle fibres. Vacuolization of the cardiac musculature due to glycogen infiltration is found normally in the Purkinje fibres. In the vicinity of foci of myocardial fibrosis similar vacuolated fibres as

seen in the beri-beri heart are frequently observed. Vacuolization is therefore not limited to the beri-beri heart although its diffuse occurrence to such a striking degree may be characteristic for the disease if the diagnosis is fully established on clinical grounds. However, caution must prevail in basing the diagnosis on the presence of such morphological findings alone.

The experiments in which beri-beri was produced in pigeons, chickens, rats and monkeys were concerned chiefly with the characteristic lesions of the peripheral nerves. Shiga and Kusama mention heart muscle fragmentation in birds and a very conspicuous dilatation and hypertrophy of the heart with hydropericardium in monkeys. McCarrison emphasizes the small heart with dilatation of the right auricle and ventricle in birds, the flabbiness of the organ and the occasional presence of a band of edema replacing the auriculo-ventricular band of fat. Shimazono also stresses the absence of heart hypertrophy or dilatation in experimental animals.

Vitamin B_2 deficiency. No significant changes have been observed in pellagra. Brown atrophy occurs as in other cachectic states, and microscopic findings of interstitial myocarditis have been reported. These are certainly not characteristic.

Vitamin C deficiency. The heart in scurvy shows, according to Aschoff and Koch, no conspicuous changes. In their series of twenty-three cases they twice found a dilatation of both ventricles with tigering, but microscopic examination revealed fatty changes in only one case. Twice an acute thromboendocarditis was present, but this was probably a terminal endocarditis. The hemorrhagic tendency in scurvy, evidenced by the multiple hemorrhages into the skin, mucous membranes, musculature, periosteum and joints leads one to expect striking vascular lesions. However, except for frequent venous thromboses, which are explained as marantic precipitations thrombi, nothing significant is found morphologically. Thus, Aschoff and Koch regard the hemorrhages as the result of diapedesis caused by abnormal vascular permeability. It is possible that the latter is determined by atrophy of the collagenous basement membrane of the smallest vessels, because the inability to form intercellular cement substance is the pathognomonic feature of vitamin C deficiency.

The heart in Moeller-Barlow's disease, generally regarded as infantile scurvy, shows much more striking changes. Erdheim reported the almost constant hypertrophy of the right ventricle as a characteristic feature in his thirty-one cases. He believes that the cause of the striking hypertrophy lies in the limited respiratory action. The latter is forced upon the infants by the painfulness of respiration due to the severe rib lesions pathognomonic of Moeller-Barlow. Because of the diminished expansion of the lungs, the blood has to be driven into the lesser circulation instead of being sucked in, as under normal conditions. This increased activity of the right heart leads to its hypertrophy. Histologic studies are lacking.

The morphologic investigations of experimental animals with vitamin C deficiency must be divided into those with pure deficiency and those in which deficiency was combined with infections. In the first group, many authors have reported extensive foci of fatty degeneration in the myocardium in experimental scurvy in guinea pigs. Höjer, to whom we are indebted for a most comprehensive monograph, describes atrophy combined with necrosis, which has a tendency to calcification. He regards these changes as the pathologic-anatomic foundation of cardiac insufficiency where it occurs as an early symptom of scurvy. Rinehart and Mettier, whose work will be discussed in more detail, found degenerative changes in the structure of the heart valves. The fibres showed thinning, fragmentation and disorganization of their regular axial arrangement. In only two cases was there observed a mild proliferative reaction of the endothelial or subendothelial cells. These authors examined the organs of animals with acute, subacute and chronic scurvy, not only when uncomplicated but also after infection (chiefly with hemolytic streptococci) had been induced. In animals with scurvy and coexisting infection there were distinct changes "fundamentally similar," according to the authors, to those of rheumatic fever, both in the heart and in the joints. Proliferative lesions associated with areas of fibrinoid degeneration were present in the valves of the heart and in the myocardium. Rinehart and Mettier have drawn rather far reaching conclusions. Because of the alleged similarity of the experimental lesions with those seen in rheumatic fever they advance the theory that a condition of vitamin insufficiency, a subclinical degree of scurvy, may be a necessary background for the development of rheumatic fever if an infection is added. Stimson, Hedley and Rose subsequently reported the production of similar endo- and myocardial proliferation, though without fibrinoid degeneration, in acutely scorbutic guinea pigs, following intra-cardiac injection of the toxin produced by a strain of hemolytic streptococci derived from a patient with scarlet fever. Schulz recently repeated the experiments, attempting to discover the effect of various definite grades of chronic scurvy, both uncomplicated and combined with spontaneous or induced chronic infections with hemolytic streptococci (recovered from a guinea pig with spontaneous lymphadenopathy). He summarizes his results in the following statements. Chronic scurvy and chronic infections with hemolytic streptococci acting synergically may induce non-purulent carditis in guinea pigs. Valvulitis with fibrinoid degeneration and an intense proliferative reaction constitute the most prominent lesions. The changes only slightly resemble those seen in cases of rheumatic fever. Chronic scurvy, uncomplicated by infection, induces proliferative lesions of minimal extent.

The interpretation of cardiac lesions depends, of course, on the critique of investigators. It was maintained by Eliasoph, Gross and Loewe in 1928 that up to that time cardiac lesions identical with those of human rheuma-

tic fever had not yet been reproduced in animals. It seems correct to state that the experiments just mentioned do not yet warrant a different conclusion.

Vessel changes were reported in experimental scurvy pointing to a weakness of the wall. This may possibly be due to atrophy of the adventitial collagen fibres and even of the basement membrane. According to Wolbach and Howe, scorbutus is a state characterized primarily by a cessation in the normal formation of intercellular substance on the part of supporting tissues.

Vitamin D deficiency: Cardiovascular changes in rickets have not attracted much attention. In severe cases with deformities of the thorax, hypertrophy of the right ventricle is observed. This is due to the diminished expansibility of the thorax and consequently, diminished expansion of the lung. Because of the decrease in the negative pressure, the blood has to be driven into the pulmonary circulation, which requires increased action of the right ventricle. Hence, it becomes hypertrophic. Kolisko and particularly Meixner have called attention to a dilatation of the left ventricle, which they observed in rhachitic children.

In experimental rickets no significant changes have been observed. It might be permitted, however, to mention briefly the severe cardiovascular lesions which can be produced by large doses of ergosterol in various animals. Such changes have been referred to as changes due to hypervitaminosis. M. Herzenberg, who has studied the effect of ergosterol summarizes her experiences in the following paragraph: "A daily dose of 10 mg. of ergosterol produces in chronic experiments (16 to 46 days) a severe disease in the rat, consisting of necrotic foci within the myocardium, diaphragm, gastric musculature, media of the aorta and the muscularis of the large and also small vessels. There is also elastica destruction. Simultaneously, an extensive calcium deposition can occur within the necrotic foci. An affinity of the elastic tissue for calcification is conspicuous. The calcification of the vascular elastica and of the necrotic muscle cells are so closely associated that it cannot be decided whether the necrosis of the muscularis or injury and calcification of the elastic fibres is primary."

Certainly, it can be said that the disease centers around the cardiovascular system and particularly around the heart. However, it has not been decided whether one should regard the calcification as the result of a hypervitaminosis or the necrosis with subsequent calcification as the toxic effect of ergosterol. Although the vascular lesions have some resemblance to human arteriosclerosis, especially to the type of Moenckeberg's medial calcification, both conditions can not be identified morphologically. Furthermore it should be remembered that similar lesions of myocardium and arterial medial necrosis can be produced by a variety of bacterial toxins and by adrenalin.

SUMMARY AND CONCLUSIONS

1. Except for the cardiac lesion in beri-beri no characteristic pathologic changes have yet been found in the cardiovascular system in the various forms of vitamin deficiency.

2. The nature of the vacuolization of the muscle fibres seen in the beri-beri heart is not yet clear.

3. Vacuolization of cardiac muscle fibres occurs in conditions other than vitamin B deficiency and can not be regarded as pathognomonic of it..

4. Further investigations are necessary to clarify the relationship between vitamin C deficiency and rheumatic fever.

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BENIGN NEOPLASMS OF THE SMALL INTESTINE COMPLICATED BY SEVERE HEMORRHAGE

Report of Two Cases; Operative Intervention and Recovery

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Recently, within a relatively short period of time, we have encountered two instances of benign tumors of the small bowel in which severe intestinal bleeding was the outstanding clinical symptom. In each case the diagnostic problem was made more difficult by reason of X-ray studies which revealed evidences suspicious of duodenal ulceration and only after exploratory laparotomy was the true cause of the bleeding discovered and eradicated.

CASE REPORTS

Case 1. * *History* (Adm. 397577). The patient, I. S., male, 57 years of age, had been well until 1932. Upon awakening one morning he had a tarry stool and while at work a few hours later he became dizzy and fainted. He was admitted to the Morrisania Hospital where X-ray studies were reported to be negative. He remained in the hospital for three weeks. He recovered from this episode of bleeding and remained well and had normal stools until a recurrence of his symptoms which necessitated a second admission to the Morrisania Hospital. His stools remained tarry for five days and he was put on a Sippy diet. While at the hospital X-ray studies were taken and a report of duodenal ulcer was made. In 1935, two months and again ten days before his first admission to The Mount Sinai Hospital, he again had tarry stools. At no time during this period did he have pain, nausea or vomiting. Between his first admission to The Mount Sinai Hospital, in June 1935 and his second in September 1936, another episode of severe melena necessitated his being taken to the Unity Hospital in Brooklyn where he remained four weeks. During this time he received four transfusions.

Examination. It was essentially negative upon his first admission to The Mount Sinai Hospital. Hemoglobin was 60 per cent; stools were guaiac positive. Gastro-intestinal X-ray examination revealed prepyloric spasm; the duodenal bulb was small and irritable and it was difficult to visualize. Fluoroscopically, it appeared irregular. The appearance sug-

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* Patient presented before the New York Surgical Society on October 27, 1937.

gested the presence of an inflammatory lesion of the duodenal bulb.   The patient was discharged with a diagnosis of bleeding duodenal ulcer.   He was advised to adhere to a Sippy regime.

Three days before his final admission (September 1936) to The Mount Sinai Hospital he again bled.   Up to the time of admission he had five tarry movements unassociated with pain, vomiting or hematemesis. Physical examination was essentially negative; the abdomen was soft, with no distention; no tenderness or masses were felt.   When first seen by me during the course of a routine abdominal palpation a firm, round, freely movable mass about the size of a lemon could be felt in the left upper quadrant of the abdomen.   It seemed to be movable and to disappear at times under manipulation.   There was some tenderness over the mass. The patient continued to have tarry stools and there was a gradual loss of hemoglobin from 78 per cent on admission to 42 per cent.   In view of the persistent bleeding and definite evidence of duodenal ulceration as diagnosed by X-ray studies it was felt that an exploratory laparotomy was justified, although it was difficult to evaluate the significance of the palpable mass, particularly as a gastro-intestinal X-ray examination was deemed inadvisable because of a persistent melena.

Operation.   The patient was explored through a median epigastric incision under gas, oxygen and ether anesthesia.   The stomach and duodenum were thoroughly explored and found to be negative.   There was no evidence on palpation of any ulceration from which the bleeding might have arisen.   The rest of the abdomen was systematically explored to discover the presence of the mass previously felt.   This was found in one of the loops of the ileum in which a tumor approximately the size of a hen's egg was clearly discernible, growing outward into the mesentery and inward into the lumen on the posterior wall (Fig. 1).   One small lymph node was found at the mesenteric margin.   The loop of ileum was resected, both ends were closed over, and a side-to-side enteroanastomosis was done. In all, a loop of six inches was resected.   The wound was closed with through and through silk tension sutures without drainage.   The patient made an uneventful postoperative convalescence and was discharged, well, nineteen days after operation.   Since discharge two years ago the patient has been symptom free.   He has regained his previous best weight and has had no recurrence of the intestinal bleeding.

The pathologic specimen consisted of a resected portion of the small bowel measuring 19 cm. in length and 6 cm. in width.   A large, moderately firm, rounded tumor was situated on the mesenteric border and infiltrating into the mesentery.   The tumor measured 7 by 6 by 6.5 cm.   On the external aspect it appeared to be round.   Part of it was white and was covered by a slightly congested serosa.   On the mucosal aspect it was found to be irregular, sessile and slightly nodular.   It was irregularly covered by small, punched-out shallow ulcerations varying from 1 to 4

millimeters in diameter. Its cut surface displayed a rather uniform white appearance. There was an area of uninvolved mucosa for a distance of 1 cm. and 3 cm. on either side of the tumor. The tumor definitely

FIG. 1. Photograph of resected ileum showing leiomyoma. Note ulceration near center of tumor giving rise to hemorrhage.
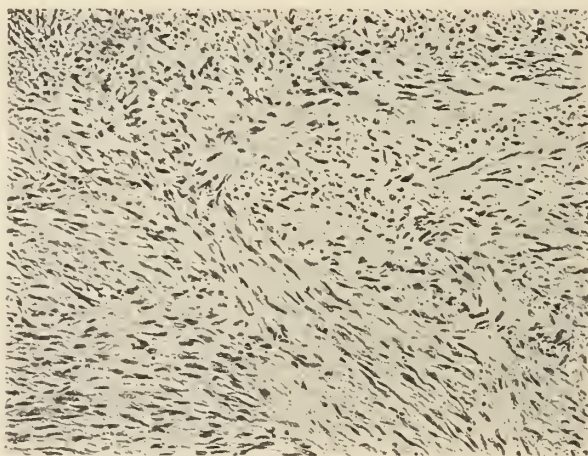
FIG. 2. Photomicrograph of leiomyoma of small intestine showing smooth muscle arranged in bundles.

constricted the lumen. The rest of the mucosa did not show any gross abnormalities. The microscopic diagnosis was *leiomyoma* (Fig. 2).

Case 2. History (Adm. 385453). The patient, S. B., female, aged 29, was admitted for the first time in October 1935 with a history that since childhood she had been subject to frequent attacks of indigestion. This consisted for the most part of epigastric pain and heartburn one to two

hours after meals. Alkalies relieved the pain but food did not. The patient discovered that a vegetable and high fat diet minimized these attacks. There were long remissions in which there were no symptoms. The patient consulted physicians three years ago at which time X-ray examinations revealed no gastro-duodenal ulceration. Four days prior to her first admission the patient fainted and two days later experienced nausea, but no pain or vomiting. Melena was noted at this time. The family noted a slight pallor. Weakness became progressively marked. Her past history was essentially negative.

Examination. The patient was an extremely pallid asthenic young woman. Her conjunctivae were pale; the tongue was dehydrated and furred. The pulse was rapid and of only fair quality. Blood pressure was 122 systolic and 84 diastolic. In the center of the epigastrium there was a localized tender area. There was no rebound tenderness; no masses or viscera could be felt. Rectal examination showed black tarry feces. Skin was extremely pallid; there was marked anemia of the nail beds. Hemoglobin on admission was 33 per cent; red blood cells 2,400,000. Patient was immediately transfused and this was repeated three days later. The stools during this time showed a strong positive guaiac reaction. There was a gradual rise in hemoglobin during the next week to 75 per cent. The patient was deemed to have a bleeding duodenal ulcer for which operation was advised. She preferred to postpone this procedure and was discharged improved two weeks later.

The patient was seen in the Follow-Up Clinic at which time gastro-intestinal X-ray pictures were taken which showed the presence of a slight but constant prepyloric incisure which, with the history of bleeding, confirmed the suspicion of a prepyloric or duodenal ulcer. A note was made, however, that the X-ray diagnosis was not a positive one. The patient gained weight, felt well and had no symptoms. Another gastro-intestinal X-ray was reported to be similar to the previous one.

Second Admission. The patient was admitted to the hospital for the second time in May 1936 with a recurrence of her previous symptoms. She was well after her first discharge until four weeks before this admission when tarry stools, progressive weakness and marked pallor recurred. There was no postprandial pain present as on the previous admission.

Examination. The patient was a very pale, apathetic white female. Lungs and heart were negative. Blood pressure was 92 systolic and 65 diastolic. Abdominal examination disclosed no abnormalities. On admission temperature was 99°F.; pulse was 112; respirations were 22. Hemoglobin was 25 per cent. Stools were strongly guaiac positive. She was given five transfusions during the first week of her stay with a rise in hemoglobin to 50 per cent. Stools continued to be guaiac positive until the end of her stay. X-ray examination of the stomach and duodenum at this time showed no evidence of an organic lesion. A barium

enema showed no abnormalities; no evidence of a Meckel's diverticulum. A sixth transfusion was administered after which the hemoglobin steadily rose to 78 per cent just before discharge. Just after admission the patient developed signs in the chest which were interpreted as pneumonic in nature. In view of the improvement in her condition and the recent respiratory infection the patient was again discharged ten weeks after admission considerably improved. When seen in the Follow-Up Clinic thereafter the patient was feeling extremely well and had no recurrence of bleeding.

Third Admission: The patient was admitted for the third time almost exactly one year after her second admission. She entered the hospital this time after having enjoyed very excellent health until three months before. On this occasion she again noticed tarry stools. She was put on a liquid diet and after a week the tarry stools became normal. One week prior to the third and last admission she began to note her stools again becoming darker. Twenty-four hours before admission she suddenly felt very faint and weak, became very pale and had an attack of syncope. There was no hematemesis or abdominal pain. Her stools were formed, although tarry. There were no noteworthy changes from previous physical examinations except for marked pallor and hypotension. The hemoglobin on this admission was 47 per cent. The patient was transfused after a further fall in hemoglobin. A Levin tube was introduced into the stomach but no evidence of bleeding could be found from this source. The hemoglobin rose after another transfusion. There was considerable improvement in spite of persistently guaiac positive stools. At the end of two and a half weeks the hemoglobin rose to 70 per cent. The next day there was a very dramatic change in the patient's condition; she again became pale and weak; her blood pressure dropped to 85 systolic and 55 diastolic; there was a rapid pulse denoting recent hemorrhage. String test at this time failed to reveal blood. This seemed to place the bleeding below the duodenum. Following another transfusion there was a marked reaction with a chill. Another chill followed another transfusion, which was followed in turn by deepening icterus, in spite of the cross matching of donors, i.e. cells of recipient with serum of donors, as well as the usual procedure of matching the cells of the donor with the serum of the patient. The liver became palpable and enlarged. It seemed that the patient had developed a hemolysin for cells of group 1. The patient's hemoglobin dropped to 34 per cent, but transfusions were withheld because of the severe reactions. Fragility of red blood corpuscles was within normal limits. Her entire stay on the medical service was marked by repeated rises in hemoglobin followed by precipitate falls due to active intestinal bleeding. After a period of about two and a half months with a hemoglobin hovering between 45 and 55 per cent it was

felt that the patient had reached the best possible condition for operation which, of necessity, would be of an exploratory nature.

Operation. The patient was explored through a median epigastric incision by Dr. L. Ginsburg under gas, oxygen and ether anesthesia. The stomach and duodenum revealed no abnormalities. Terminal ileum was then delivered and a Meckel's diverticulum was looked for. None was found and the only abnormality noted in the ileum was the adherence of a piece of omentum to a loop of ileum about two and one-half feet from the ileocecal angle. The exploration was continued by tracing the small bowel upward and finally a tumor was encountered in the jejunum about six to eight inches from the fossa of Treitz. The tumor (Fig. 3) was about the size of a cherry, sessile, occupying a base about a third of the diameter of the bowel and arose from the mesenteric side. Because of its origin from the mesenteric aspect of the bowel it was thought that it would be

FIG. 3. Photograph of resected neurofibroma of jejunum. Two areas of ulcerated mucosa giving rise to hemorrhage may be seen.

wiser to resect rather than to attempt to remove the tumor through an enterotomy. About one and a half inches of the jejunum harboring the tumor were resected. Both ends were closed. Because of the proximity to the fossa it was impossible to use clamps in performing the anastomosis and a side-to-side suture anastomosis without clamps was therefore performed. The opening in the mesentery was closed. The abdomen was closed with heavy through and through silk sutures without drainage.

The pathologic specimen (Fig. 3) consisted of a small portion of small bowel measuring 2.5 cm. in length. The serosa was smooth throughout, shining and glistening. A small gray white protruding nodule 0.5 cm. in diameter was seen to be on the mesenteric side of the bowel. Without opening the specimen the mucosa was normal except about 0.25 cm. from one end at which point there was a firm gray nodule 2 cm. in diameter almost occluding the entire lumen and attached by a broad base to the

mesenteric side of the wall. There was a superficial tract running through one portion of this nodule, which was firm and elastic, and which readily admitted a probe. The microscopic diagnosis (Fig. 4) was that of a *neurofibroma*.

The patient made a surprisingly smooth postoperative convalescence. Fortunately the temporary shock of the operation could be controlled by infusions. Her hemoglobin did not drop sufficiently to make transfusion imperative. Her hemoglobin rose steadily until, upon discharge three weeks after operation, it had reached 64 per cent. During her last hospital stay the patient received no less than fifteen citrate transfusions and was confined to the hospital for four months.
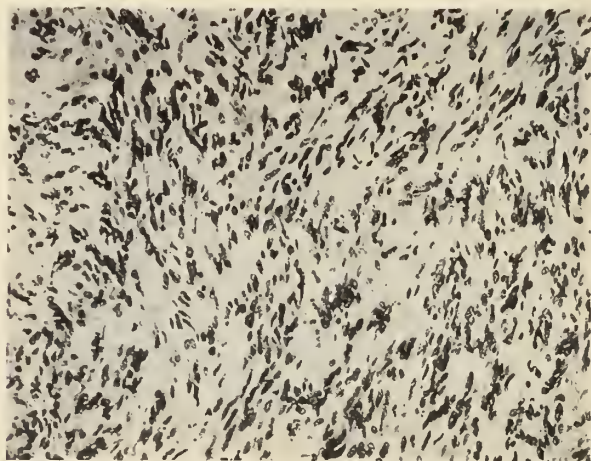
FIG. 4. Photomicrograph of neurofibroma of jejunum. Note the arrangement of the nerve cells and surrounding fibrous stroma.

The patient has not yet been seen in the Follow-Up Clinic since her most recent discharge, but it is to be anticipated that she will remain well.

COMMENT

Primary benign tumors of the small intestine are comparatively rare. In 1933 Rankin and Newell (1) collected and published the entire material encountered at the Mayo Clinic comprising, in all, thirty-five cases. It is variously estimated that primary carcinoma of the small intestine occurs approximately twice as often as do benign tumors. Just why the small intestine is relatively infrequently involved in neoplasia, as compared with the oral and terminal segments of the gastro-intestinal tract, is a moot question. For the most part benign tumors occur at a relatively earlier age than do the malign ones. The types of benign tumors found in the small intestine are polyp (adenoma), lipoma, fibroma, myxoma, myofibroma, myxofibroma, myoma, neurofibroma, angioma, endothelioma and

teratoblastoma. Polyps are encountered most commonly, with lipomata, myomata and fibromata next in point of frequency. These tumors may be either intra- or extra-luminal depending upon whether they arise from the submucous or subserous connective tissue. These tumors may give rise to symptoms during life necessitating operative intervention or they may be discovered accidentally in the course of operation for other conditions or at autopsy. For the most part, abdominal pain is the outstanding symptom and is usually the result of an accompanying complication of the tumor. The complication in over 50 per cent of the reported cases is caused by either a complete or incomplete intussusception with an attendant intestinal obstruction or due to an encroachment of the growth on the lumen.

Gross hemorrhage, the outstanding and obvious complication in the two cases herein reported, while observed and reported in the literature, is much rarer and occurred in only four cases of the thirty-five reported by Rankin. The intestinal bleeding is frequently repeated. It may be mild or severe and it is remarkable how a small ulceration of the mucosa overlying the tumor can give rise to such alarming loss of blood. It is understandable how these cases simulate bleeding duodenal ulcer and in the presence of a suspiciously positive roentgenogram the true condition is almost always overlooked. The correct diagnosis is much more likely to be made when the tumor is situated in the duodenum where X-ray examinations can usually demonstrate the lesion. The palpation of the tumor through the abdominal wall, as in Case 1, may also lead to the correct preoperative diagnosis. In those cases in which a roentgenological diagnosis of an acute or chronic intussusception in the small intestine can be made, the presence of a benign neoplasm of the small intestine can be predicated. Repeated episodes of melena in which the gastric symptoms are not characteristic of ulcer in the absence of hematemesis should direct one's suspicion to the possibility of a small intestinal neoplasm. This is particularly important because if the condition is not suspected before operation it can readily be overlooked. More refined X-ray studies of the small intestine with observations at frequent intervals following the ingestion of a barium meal will no doubt reveal more such cases.*

REFERENCE

(1) RANKIN, F. W., AND C. E. NEWELL: Benign tumors of the small intestine. Surg., Gynec. and Obst., 57: 501, 1933.

* Since this article was written another case of bleeding small intestinal tumor has been encountered.

OPERATION—A CAUSE OF CORONARY OCCLUSION

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INTRODUCTION

Realizing that the effect of surgical intervention upon the heart is of great practical importance we have been interested for some time in its relation to coronary artery occlusion. In a study of the events associated with its onset (1, 2) we concluded that coronary artery occlusion occurred irrespective of external factors, such as activity, excitement, etc., but was influenced by surgical procedures and possibly the administration of insulin. The number of attacks following operation suggested more than a coincidental relationship. Much has been written concerning the effect of operation upon the heart, particularly in precipitating heart failure. However, few authors have discussed the relation of operation to coronary occlusion, and their opinions as to the frequency of association of the two conditions are divided. A number of cases have been reported (3–8) in which an operation or a minor surgical or laboratory procedure was directly connected with the onset of coronary artery occlusion. In one hundred and ninety-two operations studied by Sprague (9), twenty-two patients died from causes referable to the heart; five of these were probably cases of coronary artery occlusion but its significance was not stressed. Fitz-Hugh and Wolferth (10) observed that coronary artery occlusion might occur during or soon after operation for calculous cholecystitis. Levine (11) found three unexpected deaths among thirty-five patients with angina pectoris undergoing operation and believes that in such patients operation may precipitate an occlusion. This opinion is shared by Harrison (12). Similarly Fishberg (13) believes that coronary artery occlusion is less rare following operation in patients with coronary sclerosis than one would anticipate if it were merely coincidental. Saphir and his associates (14) alone stressed the danger of occlusion after operation and advised minute care to avoid it.

In this report we wish to emphasize the importance of operation in precipitating coronary artery occlusion and to analyze a series of cases from the standpoint of factors leading to the occlusion.

DATA

Incidence. The series discussed here consists of thirty-one proved cases of acute coronary artery occlusion which occurred following a

surgical procedure in The Mount Sinai Hospital from 1931 to 1937 (Table I). These cases comprise 5 per cent of the total of six hundred cases of coronary occlusion observed in this hospital during these years, an incidence for postoperative attacks that we believe to be significant.

Sex. Twenty-six attacks occurred in males, and five in females, a ratio of five to one. Thus, although the number of operations performed on the female wards is practically equal to that on the male wards, males were affected five times as frequently as females. Coronary thrombosis in general (15) is found four times as frequently in males as in females, so that the ratio of the sexes is approximately the same, whether an attack occurs spontaneously or postoperatively. The danger of postoperative occlusion is less in women than in men because coronary artery disease is less frequent in the former.

Age. All but two of the patients were 50 years of age or over, and as many as two-thirds were 60 years or more; the average age for the group was 62 years. Coronary artery thrombosis in general, as determined from a series of three hundred cases (15) occurs most commonly in the sixth decade instead of the seventh; fully 30 per cent of patients are below 50 years of age and the average age is only 55 years. This suggests that coronary artery occlusion following operation is more likely to occur when there has been long-standing coronary artery disease and that whatever the nature of the operative factors leading to coronary thrombosis, they affect the old rather than the middle-aged patient.

Previous cardiac disease. A survey of the past history and clinical records of the patients confirms the impression that postoperative occlusion usually occurs in those with evidence of cardiac involvement due to coronary artery sclerosis. Clinical or electrocardiographic evidence of the latter was obtained in 74 per cent of the group and this figure would undoubtedly have been higher had more careful clinical studies been made. On the surgical and private wards, detailed medical histories and cardiac examinations were not always recorded. A positive history or physical signs of cardiac involvement were lacking in only three patients with complete clinical records among the thirty-one cases. In the cases personally observed by us, the presence of previous cardiac disease was practically universal. An analysis of all the available material reveals that many patients gave a history of typical angina pectoris or dyspnea on mild exertion and six had already suffered a coronary artery occlusion several months or years previously. Long-standing hypertension and consequent cardiac enlargement had been present in twelve patients (39 per cent).

Preoperative electrocardiograms were obtained in eleven patients; ten of them showed definite evidence of myocardial damage, such as T-wave changes with or without an abnormal QRS complex. At post mortem examination the hearts showed moderate to severe sclerosis and narrowing of the coronary vessels with fibrosis of the myocardium.

TABLE I

Thirty-one Proved Cases of Coronary Artery Occlusion Following Operation, 1931–1937

	CASE	NUMBER	SEX	AGE	OPERATION	ANESTHESIA	POSTOPERATIVE COMPLICATIONS	TIME OF OCCLUSION	SYMPTOMS OF ATTACK	OUTCOME	ECG	POST MORTEM
1	B. K.	384249	M	66	Iridectomy for cataract	Local		4 hours	Pain, cyanosis, shock	Recov.	+T-1	
2	S. Y.	332329	M	58	Ileocholectomy for Ca.	Spinal G.O.E	Necrosis of bowel, mesenteric thromb.	4 hours	Shock	Death in 8 hrs.	0	Old L. circ. Acute L. circ.
3	J. G.	381890	M	67	Tracheotomy. Laryngeal edema	Local		5 hours	Dyspnea, cyanosis, shock	Recov.	+T-3	
4	J. S.	387855	F	50	Spinal tap. Myelopathy	Local		6½ hours	Shock, vomiting, cyanosis	Recov.	+T-3	
5	V. D.	384249	M	69	Cholecystectomy, cholecystitis	Local G.O.	Peritonitis	1 day	Sudden death	Death in few min.	+T-1	Old LAD. Acute LAD
6	B. S.	409017	F	58	Resection of rectal Ca.	Avertin G.O.E.		36 hours	Shock	Death in 12 hours	+	
7	P. W.	380449	M	64	Gastrostomy. Ca. of cardia	Avertin G.O.E.	Hemopneumothorax	2 days	Pain, pulmonary edema	Death in 36 hours	+T-1	Old LAD. Acute LAD
8	D. L.	388426	M	72	Tracheotomy. Ca. of larynx	Local	Gastroenteritis	2 days	Pain, weakness	Death in 19 days	+T-1	
9	I. C.	375849	M	74	Cholecystostomy, cholecystitis	Local G.O.E.	Localized peritonitis	1 day	Dyspnea	Death in 2 days	0	Acute L. circ.
10	J. H.	404055	M	75	Suprapubic cystostomy	Local	Cystitis	2 days	Pain, dyspnea	Death in 2 days	0	Myomalacia. Marked sclerosis
11	S. G.	404600	M	67	Laparotomy. Perforated ulcer	Spinal	Thrombosis of gastro-duodenal artery	3 days	Pain	Death in 6 weeks	+T-3	Acute L. circ.

12	J. N.	395230	M	82	Suprapubic cystostomy	Uremia, broncho-pneumonia	Local	3 days	Dyspnea	Death in 1 day	0	Acute L. circ. Acute R. circ.
13	J. D.	342717	M	50	Paravertebral block-angina		Local	3 days	Pain, shock	Death in 4 hours	+T-1	Old LAD. Acute LAD
14	H. S.	353919	M	57	Vas ligation prost. hyp.		Local	3 days	Pain	Recov.		
15	H. G.	361738	M	66	Release ventral hernia	Intestinal obstruction	Spinal	3 days	Dyspnea, cyanosis, shock	Death in 30 hours	+T-1	Old LAD, L. and R. circ. Acute L. circ.
16	S. H.	341642	M	64	Prostatectomy	Septicemia	Spinal	4 days	Pain, dyspnea, shock	Death in 5 days	0	
17	A. B.	332962	M	62	Prostatectomy		Local	5 days	Cyanosis, weakness	Death in 9 days	+	
18	L. B.	402787	M	66	Transurethral vasectomy		Spinal	6 days	Pain, dyspnea	Recov.	+T-3	
19	H. P.	373861	M	63	Nasal polypectomy		Local	7 days	Pain	Recov.	+T-1	
20	L. M.	403630	M	70	Tracheotomy. Ca. of larynx	Supp. broncho-pneumonia	Local	8 days	Dyspnea, cyanosis	Death in 1 day	0	Acute R. circ.
21	B. F.	377318	M	65	Suprapubic cystostomy. Fulguration ca.	Pyelonephritis	Spinal	8 days	Dyspnea, shock	Death in 12 days	+T-3	Acute L. circ.
22	E. S.	346631	F	70	Mastoidectomy		Ether	9 days	Pain	Recov.	+T-1	(1 year later), rt. cor.
23	B. F.	407310	M	44	Ileostomy; T.B. enteritis	Peritonitis	Spinal	9 days	Dyspnea, cyanosis, shock	Death in 12 hours	0	Acute rt. cor.
24	I. P.	403569	F	55	Thyroidectomy. Adenoma		Avertin G.O.E	10 days	Pain, dyspnea	Recov.	+T-3	
25	J. S.	380637	M	73	Cholecystectomy. Hepatitis	Cholangitis	Ethylene	10 days	Pain, dyspnea	Death in 2 days	+	Acute LAD

TABLE I —*Concluded*

CASE	NUMBER	SEX	AGE	OPERATION	ANESTHESIA	POSTOPERATIVE COMPLICATIONS	TIME OF OCCLUSION	SYMPTOMS OF ATTACK	OUTCOME	ECG	POST MORTEM
26	I. F.	391201	M	56	Orchidectomy. Sarcoma	Spinal G.O.E.		10 days	Shock, dyspnea	Death in 12 hours	0	Myomalacia. Luetic ostial stenosis
27	S. J.	392020	M	51	Incision gangrene of foot	G.O.	Progressive gangrene	10 days	Shock, cyanosis	Death in few min.	0	Myomalacia. Pulm. emb.
28	L. G.	405109	M	46	Inguinal herniorrhaphy	Spinal	Bronchopn.	13 days	Pain	Recov.	+T-1	
29	N. R.	411760	M	63	Prostatectomy	Spinal	Pyelonephritis	13 days	Pain, cyanosis, shock	Death in 1 day	+T-3	Myomalacia. Severe sclerosis
30	M. R.	358114	F	56	Gastrectomy, hypertrophy	Spinal	Abscess of stump and liver	18 days	Pain	Death in 8 days	+T-1	Acute LAD
31	J. D.	399056	M	60	Resection rectal ca.	G.O.E.	Cerebral metastases, bronchopn.	21 days	Shock, dyspnea, cyanosis	Death in 1 day	+	

Time of onset of occlusion.   The time of onset of the attack following the surgical procedure was determined in each case.   Six attacks occurred within twenty-four hours postoperatively, four occurred on the second day and five on the third, making a total of fifteen attacks (48 per cent) occurring within three days of the operation.   Three attacks began on the fourth to the seventh, eleven during the second week and the remaining two during the third week.   One case in which the attack occurred six weeks following cholecystectomy was not included in this series.

The fact that one-half the attacks occurred within three days following the operation is significant; it is reasonable to assume that in these cases the occlusion was related to the immediate effects of the operation.   In the remaining attacks, particularly those after the first week, the association is less direct.   We feel, however, that even in these cases, the operation or factors resulting from it may be responsible for or conducive to the formation of the coronary thrombosis or myocardial infarction.

Exact data on the length of time necessary for the formation of a thrombus in a coronary artery in man is lacking, although recent clinical observations show that preliminary pain and premonitory symptoms may occur several days or even weeks before the actual clinical attack of occlusion.   It is possible that the thrombus may be in the process of formation during this period of premonitory symptoms.   If so, the occurrence of a thrombosis as late as a week or more after an operation does not exclude the operation as the precipitating factor.

Types of operations.   All types of operations were represented in the series from the simplest to the most formidable.   Since the majority of patients were 60 years of age or over, most of the operations were performed for conditions apt to be present in an older age group.   There were eleven abdominal operations, such as cholecystectomy and gastric, colonic or rectal resection for carcinoma.   Nine patients were operated upon for a genito-urinary condition, particularly first or second stage prostatectomy.   Three operations involved the eye (iridectomy), ear (mastoidectomy) or nose (polypectomy) and in three patients a tracheotomy for edema or carcinoma of the larynx was performed.   Other miscellaneous procedures included thyroidectomy, inguinal herniorrhaphy, and drainage of a phlegmon and gangrene of the foot.   Two attacks occurred following such simple procedures as a spinal tap and paravertebral block.   In the presence of this high incidence of prostatectomies or vas ligations in old men, it is interesting to note that no attack of occlusion was observed on the gynecological ward, where pelvic operations are performed on women in the same age group.

Duration of operation.   The duration of the operations varied from ten to fifteen minutes in paravertebral block or vas ligation to several hours in gastrectomy.   Twelve lasted one-half hour or less, nine from one-half to one hour and nine from one to two hours.   One operation

(gastrectomy) lasted as long as three and a half hours. These figures indicate that the occlusion was as liable to occur after short and simple operations as after long and complicated ones.

Anesthesia. Local anesthesia with novocaine was employed in eleven cases, spinal anesthesia in nine cases and inhalation anesthesia with nitrous oxide, ether or ethylene in four cases. Inhalation anesthesia was combined with local anesthesia twice, with spinal anesthesia twice and with avertin three times. Thus local anesthesia was used thirteen times, spinal anesthesia eleven times, inhalation of nitrous oxide or ether eleven times, and avertin three times. Postoperative coronary occlusion was found, therefore, following all types of anesthesia and since the effect of anesthesia on the circulatory dynamics differs with each agent employed, it is difficult to accept all of them as factors conducive to thrombosis.

Postoperative shock. There was moderate to severe immediate postoperative reaction (rapid pulse, low blood pressure, cold clammy skin, profuse perspiration, cyanosis, etc.) in nine patients, and a mild reaction in ten others. Thus, some degree of surgical shock existed in 60 per cent of the group. The occlusion did not necessarily occur during the stage of shock; in eight of the cases it appeared after the third day when the patient had recovered from the immediate effects of the operation; in five it occurred during the first twenty-four hours while some degree of shock was still present.

Intravenous fluids. Following the operation fluids were administered intravenously by the continuous drip method to nine patients. The average duration of administration was from one to three days and the total amounts of fluid given ranged from 1000 to 2000 c.c. daily. In eight of the nine patients the occlusion occurred during or soon after the intravenous infusion. It is well known that the rapid administration of fluids to individuals with myocardial weakness often precipitates cardiac failure by increasing the venous return to the heart, but that this factor is also associated with the formation of arterial thrombosis is not probable. In fact, theoretically, it might be considered that the fluids prevent dehydration and therefore mitigate the likelihood of coronary artery thrombosis.

Bed rest. In surgical cases bed rest and immobilization of the body is an important factor in the formation of peripheral venous thrombosis leading to pulmonary embolus. To determine whether it was of similar importance in our series the total bed rest of each patient before the coronary occlusion was estimated. In seven patients who had been ambulatory up to the time of operation the attack occurred on the day of operation, so that bed rest need not be considered a factor. In seven patients the duration of bed rest, both pre- and postoperative, before the onset of the attack, was only one to five days and in four patients it totalled one week. Two-fifths of the groups were confined to bed for more than one week. The longest bed rest was seven to nine weeks.

Clinical diagnosis. In most cases the coronary occlusion was manifested clinically by the sudden onset of shock, dyspnea and cyanosis. Sudden shock was the most frequent symptom and usually dominated the clinical picture. Chest pain which was present in only thirteen or two-fifths of the patients was not so striking a symptom as it usually is in coronary artery occlusion. For this reason the clinical differentiation of postoperative coronary occlusion from pulmonary embolism is difficult since the signs and symptoms may be the same in both conditions. Cases dying presumably from pulmonary embolism were found at necropsy to have acute coronary artery occlusion and vice versa. We did not accept, therefore, the clinical diagnosis of coronary occlusion unless it was confirmed by characteristic electrocardiographic changes or post mortem examination.

In a few cases the occlusion was not suspected during life and was found only at post mortem examination. In these instances it was silent or the symptoms were masked by other postoperative complications such as bronchopneumonia, uremia and cholangitis (Case № 12,20,25).

Electrocardiographic diagnosis. In nineteen cases electrocardiograms were obtained postoperatively and following the onset of the attack. With one exception they showed acute changes diagnostic of coronary occlusion. Seven records presented a T-1 pattern characteristic of anterior wall infarction and eight a T-3 pattern characteristic of posterior wall infarction. In three records, although acute changes occurred, they were atypical and accurate localization of the infarct was impossible. The situation of the infarct in this series does not differ from that in our larger unselected series (15) in which T-1 and T-3 patterns occurred with equal frequency.

Electrocardiograms showing changes resembling those seen in pulmonary embolism were excluded unless the diagnosis of coronary occlusion was confirmed by necropsy. Such changes as a large S-1 and Q-3 and elevated R-T transition and inverted T-wave in lead III seen in pulmonary embolism may also occur in posterior wall infarction. The electrocardiographic differentiation is often impossible.

Mortality rate. Twenty-two (71 per cent) of the thirty-one cases of postoperative coronary thrombosis ended fatally, a very high mortality rate, in contrast to the average mortality of 30 per cent on the medical wards of the same hospital during the same period of years (15). It must be remembered, however, that the actual mortality rate in postoperative occlusion may be lower than this figure indicates since several cases that survived the attack were excluded from our series because of lack of post-mortem confirmation of the diagnosis. Yet even after taking this factor into account, we believe the mortality rate of postoperative cases to be about twice the ordinary mortality rate.

Causes of death. The coronary occlusion or resulting heart failure was the direct cause of death in eight of the twenty-two fatal attacks. In the remaining fourteen, other postoperative complications, often fatal even

in the absence of a coronary artery occlusion, were present. These associated complications included bronchopneumonia, uremia, pyelonephritis, peritonitis, cholangitis, bowel necrosis, intestinal obstruction, cerebral metastases and septicemia. In case number 27, sudden death was due to both myocardial infarction and pulmonary embolism. Although several attacks following simple operative procedures, such as suprapubic cystostomy, ended fatally, most of the deaths occurred in patients who had undergone the more serious operations, such as gastric or rectal resection and cholecystectomy. In these cases it was often difficult to determine whether the severe operation, the underlying disease for which the operation was performed, or the coronary occlusion was the direct cause of death. Usually it was a combination of factors.

Death following the attack of coronary artery occlusion was instantaneous in two patients. In seven it occurred on the first day of the attack, and in six on the second day. In eighteen of the twenty-two fatal attacks death occurred within one week of the onset. The associated postoperative complications were found in cases of both early and late death. For example, in case number 5, in which sudden death was caused by a coronary occlusion, there was also peritonitis due to a ruptured gall-bladder which probably would have been rapidly fatal. On the other hand case number 29 survived the coronary occlusion for eight days but death occurred from perforation and abscess formation in the gastric stump.

Post mortem findings. Post mortem examination was obtained in eighteen cases. In fifteen the diagnosis was definite or suspected during life and in three the post mortem findings of coronary occlusion and myocardial infarction were totally unexpected (Case # 12,20,25).

The acute thrombosis was situated in the left anterior descending artery in five hearts, in the left circumflex artery in five hearts and in the right coronary artery in four. One heart showed thrombosis of both the left and right circumflex arteries. Thus the infarction was situated on the posterior wall twice as often as on the anterior wall of the left ventricle, a finding similar to that observed in a previously reported unselected series (16). However, the present series differs from the latter in two respects. First, there was but one instance of multiple acute thrombi, whereas in almost two-fifths of the unselected series acute thrombosis was present in more than one artery. Second, old occlusions were present in only 23 per cent of the eighteen hearts as compared to 85 per cent in the previous series. In other words, death from a single thrombosis is rare in the average case of coronary occlusion but is common in postoperative cases. Apparently these patients cannot withstand the effects of a single infarct when it is combined with other factors related to the operative procedure, or possibly the explanation may lie in the fact that patients with postoperative coronary occlusion die before thrombosis can develop in another artery.

In one case acute myomalacia of the posterior wall resulted from complete stenosis of the right coronary ostium and partial occlusion of the left ostium. The clinical attack was typical in every way of coronary artery occlusion due to acute thrombosis.

Two hearts presented acute infarction of the myocardium but no actual thrombosis could be found, although the coronary vessels were markedly sclerotic and narrowed. The infarction apparently resulted from a sudden diminution in coronary blood flow following the operative procedure. The various factors responsible for this will be discussed later.

DISCUSSION

Study of the mechanism by which operation leads to coronary artery occlusion in susceptible persons is of both practical and theoretical value if this accident is to be prevented and knowledge of the formation of coronary occlusion in general obtained. We have found that occlusion may occur after all types of operation and anesthesia. It followed simple, short operations as well as extensive ones. Apparently rest in bed is of little significance since the occlusion not infrequently took place on the day of operation in patients previously ambulatory. Furthermore coronary occlusion is extremely rare on the medical wards, in spite of prolonged stay in bed for conditions such as carcinoma, chronic infections, etc.

Thrombosis in general has been attributed to three conditions: disease of the wall of the vessel, changes in the physical and chemical properties of the blood, and alterations in the circulatory blood volume and speed of blood flow. The first of these, namely disease of the vessel, was present in all of our cases of postoperative occlusion, each of which gave clinical or anatomical evidence of coronary sclerosis. The second and third conditions might easily ensue from operation and the administration of an anesthetic. In two-thirds of our cases the operation or anesthesia was accompanied by a state of surgical shock with a drop in blood pressure resulting in a reduction in circulating blood volume and retardation of blood flow. The venous return to the heart, and therefore the cardiac output, are in such cases diminished. Since the circulation in the coronary arteries depends upon the cardiac output and the pressure in the aorta, the amount of blood going through the coronary arteries is reduced, favoring the formation of a thrombus or myocardial infarction (12, 17). It will be recalled that there were two instances in our series in which myomalacia was found at necropsy in the absence of occlusion. In one of these severe shock had developed during the operation and it is probable that the fall in blood pressure was sufficient to produce ischemia of the myocardium with infarction. It is an interesting point that only 40 per cent of our postoperative cases had preceding hypertension whereas 70 per cent in the total series (15) of coronary artery occlusion gave such a

history. This disparity may be explained on the basis of the fact that fewer operations are performed in persons with hypertension, or it may be that when hypertension is present the blood pressure at operation does not usually drop to a level comparable to that in cases without hypertension, and therefore occlusion does not take place. However, our series is too small to draw definite conclusions.

Tachycardia, often present both preoperatively and postoperatively, is another factor which may contribute to the formation of coronary artery occlusion and myocardial infarction. When the rate rises above 120 or 140 beats per minute, an added burden is placed on the heart. If the coronary circulation is already reduced as a result of coronary narrowing and a drop in blood pressure, the additional strain may increase the coronary insufficiency and lead to thrombosis.

Some degree of dehydration attends the majority of operations. If severe, it may be a factor in the formation of coronary thrombosis (18), since it produces a diminution in blood volume, as well as changes in the composition of the blood. There is probably also an increase in its viscosity.

The relation of traumatization of tissues during operation to coronary occlusion is probably not significant. However, if the manipulation of tissues is extensive, chemical substances of a histamine-like nature may be liberated and produce changes in the blood including the coronary circulation.

Finally the possible rôle of infection in the causation of coronary occlusion must be considered. In the large general series of coronary occlusion previously mentioned (1, 2) infection was very rarely associated with an attack, and when present was of a mild nature. We concluded, therefore, that it was not significant. In many of the postoperative cases, however, suppuration of severe grade developed and it is possible that in these the infection played an accessory rôle in the formation of the thrombus. We do not believe that it was the sole or chief factor. In some cases there was no evidence of infection.

It is apparent that any discussion of the relationship of operation to coronary artery occlusion must be, at present, largely theoretical. The problem requires a great deal of intensive study which should include complete histories and physical examinations of the cardiovascular system, electrocardiograms and preoperative and postoperative observations of the vital capacity and velocity of the blood flow. The blood pressure should be recorded frequently during and immediately after the operation. A comprehensive investigation of the blood to include blood volume, hematocrit reading, platelets, hemoglobin, total protein and coagulability should be made before and after operation. By following changes in all of these factors it may be possible to obtain a clue to the relationship of

operative procedures to thrombosis and occlusion of the coronary arteries. At present, detailed anatomical studies are being carried out in conjunction with the Department of Pathology to determine the exact method of formation of the occlusion, particularly the relative frequency and importance of subintimal hemorrhage or actual thrombosis as a cause of the occlusion. Finally, experimental studies, such as those described by Hall, Ettinger and Banting (19), should be pursued further. These investigators have produced coronary thrombosis and myocardial infarction in dogs by repeated injections of acetylcholine.

SUMMARY

Thirty-one attacks of coronary artery occlusion occurred following operations performed in The Mount Sinai Hospital during the years 1931 to 1937. These comprised 5 per cent of the total number of attacks cared for in the hospital during this period.

The distribution of attacks between the sexes was similar to that in spontaneous coronary occlusion, about five times as frequent in men as in women.

All but two patients were fifty years of age or older. Two-thirds were between sixty and seventy years.

Every case probably had previous coronary artery disease.

The occlusion occurred in the first three postoperative days in half the cases. All but two occurred in the first two weeks.

The occlusions followed all types of operation and anesthesia. The duration and severity of these varied widely.

Postoperative surgical shock was present in 60 per cent of the cases.

Bed rest was not a factor in the onset of an attack.

Postoperative occlusion is characterized by shock, dyspnea, and cyanosis. Because of the similarity of the symptoms to those observed in pulmonary embolism, only proved cases of coronary artery occlusion were accepted for this paper.

Seventy-one per cent of the patients died. In eight cases the fatality was caused solely by the occlusion. In the remaining cases surgical complications were associated with the heart condition.

The mechanism of the formation of coronary occlusion following operation is discussed. The factors include tachycardia; surgical shock with diminution in blood volume, drop in blood pressure, and reduction in coronary flow; alterations in the chemical and physical properties of the blood; dehydration; infection; toxic effects of anesthetics.

In patients over forty-five years of age the presence of coronary artery disease should be diligently searched for before operation. When coronary sclerosis is present, the question of surgical intervention and the choice of surgical procedures should be carefully weighed.

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THE LATENT OR ALBUMINURIC PHASE OF GLOMERULONEPHRITIS

Report of a Case of Thirty-Five Years Duration

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Acute glomerulonephritis has a varied and often prolonged biological course. The study of the different ways this disease evolves is largely within the prerogative of those practitioners who are in the fortunate position to follow this malady from its very beginning. Those who work exclusively in hospitals are at a disadvantage because they observe the disease usually only in the middle or terminal phases, and the evolution can only be reconstructed by clinical data which are often incomplete. In a paper published in 1930 (1) I tried to enumerate the various clinical evolutions of glomerulonephritis. Ordinarily, after an interval of between two and four weeks after streptococcus infection, the typical signs and symptoms of glomerulonephritis appear. Unless signs of left heart failure and, less frequently, of azotemia appear, the patient progresses to recovery within a few weeks. Usually the last sign to disappear is the albuminuria. In my experience, albuminuria persisting after the third month always means that the disease is passing into the chronic stage. This is an exceedingly common sequence and accounts for many of the persistent albuminurias found in adolescents and the early middle years of life. The diagnosis in these cases is often difficult because hypertension is so frequently absent. This does not imply that hypertension was always absent; it may have been present in the early phases. These patients present no evidence of renal insufficiency, except nocturia, indicating a certain loss in concentrating power. The disease is readily differentiated from orthostatic albuminuria by the finding of persistent albumin in the morning urine. Practically the only sign of the disease is the persistent albuminuria and these patients seek medical advice for one reason only, namely, that they have been rejected for life insurance. The amount of albumin in the urine is nearly always a mere trace; when the albumin amounts to more than one gram per liter or more (Linder, Lundsgaard and Van Slyke (2)) the nephrotic or hypoproteinemic phase soon appears and colors the clinical picture profoundly. It is not sufficiently appreciated that this albuminuric or latent phase of chronic glomerulonephritis may persist for many years. Up to the present the longest period I have observed was in a patient whom I had observed over a

period of twenty-two years, from 1907 to 1929. The following case is reported because it bears strong clinical evidence that the disease lasted thirty-five years.

History. B. G., aged 40, was admitted to The Mount Sinai Hospital on November 27, 1935. The family history is irrelevant. The patient had had scarlet fever thirty-five years ago. He recalled swelling of the body at that time and was told that he had "kidney trouble." He had voided six to seven times daily as long as he could remember, and had had nocturia (once or twice) for many years. There was no hematuria. He had had occasional puffiness of the face for many years. Fifteen years before he was refused life insurance because of albuminuria. The blood pressure at that time was normal. He had tried to get life insurance on several occasions since, but never succeeded because of the persistent albuminuria. He said that his urine was always pale. He denied having had gonorrhea and syphilis by name and symptom. The patient felt well up to two years before admission. At that time, while standing, he experienced a fairly severe transitory cramp in the right calf muscle. His physician discovered at that time a systolic pressure of 200 and albumin in the urine. Shortly thereafter, episodes of spasmodic contractures of the hands and feet began to occur. They appeared about once in two months, sometimes awakening him from sleep. One year before admission he developed an itching crusted skin lesion in both armpits and on the penis. This gradually disappeared spontaneously in several months. At the same time, the episodes of carpopedal spasm began to occur more frequently and occurred at the time of admission to the hospital at least once a week. He also began to have two or three stools daily, of normal appearance. During this period he noted a progressive loss of weight and anorexia. Six months before admission he began to have morning nausea. At the same time he noted dyspnea on exertion. He occasionally saw spots before the eyes. He had no headaches. There had been a loss of libido during the past year.

Examination. The patient was pale and sallow. There was slight exophthalmos. The fundi showed pale discs with clear margins. The arteries were narrowed with a high light reflex. There were a few scattered linear hemorrhages in the retinae and fewer hard appearing exudates. The chest was emphysematous. The heart was enlarged to the left. The sounds were of good quality. The aortic second sound was louder than the second pulmonic and there was a regular gallop rhythm. The radial arteries were sclerotic and the blood pressure was 220 systolic and 140 diastolic. The liver dulness extended to one finger below the right lower costal margin. There was no ascites. The peripheral pulses were patent. The reflexes were hyperactive. There was no Chvostek or

Trousseau sign. The urine contained one gram per liter albumin. There was some loss of concentration, the highest specific gravity during his stay at the hospital being 1018. The blood showed 65 per cent hemoglobin; red blood cells 3,200,000; white blood cells 11,900; polymorphonuclear leucocytes 75 per cent; lymphocytes 17 per cent; monocytes 2 per cent; eosinophiles 6 per cent. The venous pressure was 22 cm.; on pressure over the right upper quadrant it rose to 28 cm. During his stay at the hospital the lowest systolic blood pressure was 192 and the lowest diastolic 118. The blood urea nitrogen on admission was 74 mgm. per 100 cc. The creatinin was 12.0 mgm., the cholesterol 295 mgm., the blood sugar was 95 mgm. The blood calcium was 7.2 mgm., the phosphorus 6.6 and the blood chlorides 600 mgm. per 100 cc. The total blood protein was 6.3 per cent, of which the albumin was 4.7 per cent and the globulin 1.6 per cent. The electrocardiogram showed slurring of the QRS complex, and diphasic T1 and T2 waves.

He was discharged on Dec. 17, 1935 with a diagnosis of chronic glomerulonephritis.

Readmission. He was readmitted on April 14, 1936. He was up and about at home and felt fairly well until two months before admission when he developed an itching eruption on the arms, chest, and thighs. He vomited from time to time and during the previous month vomited daily and had frequent attacks of singultus. He passed only small quantities of urine for the previous two months and since the day before admission had passed a small amount of urine on only one occasion. He had been drowsy, but could not sleep well at night. During the two months before admission the face, scrotum and ankles became swollen.

Examination. In addition to the findings on the previous admission, there were haziness of the disc margins, evidences of fluid in both pleurae, ascites, and pitting edema of the sacrum and legs. The blood pressure on admission was 180 systolic and 100 diastolic. The venous pressure was 16 cm. The heart showed a gallop rhythm. The urine concentrated to a specific gravity of 1012, and the albumin was abundant (1½ grams per liter). The blood urea nitrogen on admission was 150 mgm. per 100 c.c. The creatinin was 18.0 mgm.; the blood calcium, 5.1 mgm.; the phosphorus, 9.2. The total protein was 6.3 mgm. per cent, of which the albumin fraction was 4.3 and the globulin 2.1. The chlorides were 655 mgm. The blood carbon dioxide was 24.5 volumes per cent. Five days before death the blood creatinin was 24.0 mgm. and the urea 156.6. The patient grew more stuporous and died on April 28, 1936. Post mortem examination was not permitted.

Summary. The case presented is that of a man aged 40 who had scarlet fever thirty-five years ago complicated by renal disease with puffiness of the body. This was followed by a persistent nocturia. There is every probability that in all this period he also had a persistent albumi-

nuria, because fifteen years ago, at the age of 25, he was rejected for life insurance. At that time he apparently had no hypertension. About two years ago, symptoms and signs of renal insufficiency developed with marked hypertension and clinical evidences of tetany. Slowly signs of cardiac failure and azotemia appeared and finally death occurred in uremia.

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ERYTHEMA CRISES OF THE VISCERAL GROUP

Report of Six Cases

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Urticarial lesions of the viscera, giving rise to abdominal or chest crises, present a difficult problem in differential diagnosis, in which errors often lead to unnecessary surgical intervention.

The symptom complex, now known as erythema crises of the viscera, was first described by Willan (1) in 1808. Henoch (2) in 1868, and again more fully in 1874 (3), described a group of cases which still bears his name. The group of twenty-nine cases described by Osler (4, 5, 6 and 7) is remarkable in that the percentage of correct diagnoses was so high. This was due to the fact that even though most of them were not immediately diagnosed, they were observed long enough to enable the correct nature of the trouble to be recognized. Other groups of cases have been described by Solomon Solis Cohen (8) in 1910, Christian (9) in 1917 and Trimble (10) in 1931.

By most internists the disease is considered as an angioneurosis whose manifestations are produced by some metabolic toxin. Allergic sensitivity to foods and bacterial metabolites undoubtedly plays an important rôle in the causation of this phenomenon. The source of the toxin may be endogenous or exogenous, and is often not demonstrable. The disease is characterized by polymorphic skin lesions, in most instances associated with a variable number of visceral manifestations and occasionally with arthritis. The visceral manifestations comprise the so-called gastrointestinal crises, pericarditis, acute nephritis and hemorrhages from the mucous membranes. Recurrences are common, and each attack may be characterized by a different set of symptoms. This dissimilarity of symptomatology makes the recognition of the condition very difficult, for, even with a definite history of a former attack, and the preceding etiologic factor at hand and active, nevertheless, the second instance may in no wise resemble the first.

Six cases of this group have come under my observation. The correct diagnosis was made twice. Three patients were unnecessarily operated upon.

CASE REPORTS

Case 1 was a girl, twenty-two years of age, who had an attack characterized by a sudden onset of generalized cramp-like abdominal pain,

without nausea, vomiting or fever, or any tendency to localization. One week before there was a similar episode. There had been no joint pains or skin rash noticed. The girl seemed to be in great pain, had a distended and generally rigid abdomen, with rebound tenderness in the right iliac fossa and a well marked Meltzer sign. The temperature was 101.2°F. and the pulse 136 per minute. She had a total white cell count of 11,800 with 80 per cent polymorphonuclear leucocytes. The urine did not contain red blood cells. She was seen by a surgeon who concurred in the diagnosis of acute gangrenous appendicitis and advised operation. This was performed and the entire intestinal tract was found to be congested and edematous. The appendix was involved in the same process, but the mucosa was normal. The abdominal cramps and vomiting persisted for two days after operation. On the third day she developed a diffuse scarlatiniform eruption with scattered urticarial lesions and dermatographia. The correct diagnosis then became apparent.

Case 2, a young girl, gave a history of previous attacks of generalized abdominal pain and vomiting. In the most recent attack, however, the pain was localized in the right iliac fossa, where she had tenderness and rigidity. The blood examination showed a total white cell count of 16,000 and a polymorphonuclear percentage of 85 per cent, which are unusually high figures for these cases. The temperature was 100°F. and the pulse 124 per minute. A normal appendix was removed. Two days later a diffuse erythema with scattered hemorrhagic spots appeared.

Case 3 is most interesting inasmuch as the diagnosis was made by examination of the appendix. The patient, an eighteen year old girl, had never been ill. Her illness began suddenly, four hours before she was seen, with abdominal cramps, localized for the most part in the hypogastrium. She had vomited four times. The temperature was 101°F. and the pulse 140 per minute. Her prostration was very marked; she was restless and moaning as if in great pain. The abdomen was distended and rigid and the hypogastric region gave the appearance of a full term pregnancy. Rectal examination gave no evidence of a pelvic mass. It seemed to me that the most likely diagnosis was that of an ovarian cyst with a twisted pedicle. The surgeon who saw the girl thought, however, that, as no mass could be palpated by rectum, the patient was probably suffering from a gangrenous appendix, situated in the pelvis. Both diagnoses were erroneous. At operation the entire intestinal tract was edematous and intensely congested. The mucosa of the appendix was studded with pin-point hemorrhages, not localized to the position of the clamp. The diagnosis was made on this finding. On the second day after operation, the patient developed a generalized erythema and urticaria. The skin manifestations and abdominal cramps persisted for one week.

Cases 4 and 5 were children of five and four years respectively. The older of the two had been vomiting for one week and had complained of diffuse abdominal pain. The temperature was only 100°F. and there were

no signs of an acute inflammatory process in the abdomen. The next day the child developed a generalized urticaria. She received two doses of adrenalin intramuscularly, each of three minims within an interval of two hours. Two hours after the last dose the rash and pain disappeared simultaneously. In the other child the history was again that of an acute abdominal surgical condition and operation had been advised. When I saw the child, however, the rectal temperature was 99.8°F. and over the lower abdomen were a number of large wheals, which had apparently only recently made their appearance. A cathartic cleared up all the symptoms.

Case 6 was a man, forty-two years of age, who had had a severe upper respiratory infection in the late winter months. At no time was there any pulmonary involvement. About ten days after he was apparently well, he developed severe coughing attacks which were followed by expectoration of either blood-tinged mucus or two to six ounces of blood. Roentgen examination of the chest revealed nothing. Examinations of the sputum for spirillae and tubercle bacilli were negative. The paroxysmal nature of the cough made us suspect pertussis. The blood examination showed a total white cell count of 9,200 and a differential count of 76 per cent polymorphonuclear leucocytes, 23 per cent small lymphocytes and 1 per cent eosinophiles. It was suggested that the attacks were allergic in nature, following a sensitization to the original infection. The accessory nasal sinuses were clear. Adrenalin injections given during the seizures failed to modify them. Bronchoscopy showed the tracheal mucosa to be congested, edematous and studded with pin-point hemorrhages. Down to the point of the bifurcation the bronchial tree was negative. A vaccine was made from the tracheal secretion and administered subcutaneously for one month. Since that time the bleeding has stopped. Whether or not the vaccine succeeded in desensitizing this patient is problematical, but before its use the attacks continued unabated for a period of ten weeks.

DISCUSSION

Little is known of the pathology of the condition, except that it consists of an exudation of one or more blood components or of hemorrhages into the mucous membrane and serous coats of the viscus involved. The disease is usually more common in males and occurs almost exclusively during childhood and early adult life.

Depending on the type of attack, one or another group of symptoms may predominate. In one attack skin lesions alone may be present, while in another, one or other of the various crises may make their appearance. The skin lesions encountered consist of various forms of erythema, macules, papules, vesicles, wheals, hemorrhages, and, in rare instances, even necrotic areas due to breaking down of the hemorrhagic zones. The skin lesions are often scanty and transient and easily overlooked.

The crises in their order of frequency are:

1. Gastro-intestinal, characterized by severe general cramps, at times localized in the epigastrium or right iliac fossa, associated with nausea, vomiting and even hematemeses. They are most often mistaken for gastric ulcer or appendicitis. Diarrhea and bloody stools have been reported.

2. Renal crises with the onset of an acute nephritis give a picture very much like that of an attack of renal colic due to stone. Complicating acute nephritis with uremia has been noted.

3. Profuse bleeding from the nostrils and bronchial mucosa occurs, the latter condition often leading to a suspicion of pulmonary tuberculosis.

The temperature in these cases is usually between 100° and 101°F. The white blood count does not generally go above 12,000, with a polymorphonuclear percentage of 80 per cent. The spleen is enlarged in about 5 per cent of all cases. Cases have been reported with edema of the glottis, pericarditis and cerebral hemorrhage as complications. Intussusception occasionally occurs.

The mortality is about 20 per cent, due in most part to uremia resulting from an acute nephritis. Recurrences are common, succeeding attacks often being entirely dissimilar. The differential diagnosis is difficult.

The condition is most often confused with, in their order of frequency, acute appendicitis, penetrating or perforated gastric ulcer, renal colic due to a stone, intestinal obstruction, and, occasionally, scarlet fever. If the condition is borne in mind, a careful history relative to skin and joint manifestations in previous attacks and close scrutiny of the skin during the period of observation may avoid an embarrassing error in diagnosis.

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VALUE OF THE STERNAL PUNCTURE IN THE DIAGNOSIS OF MULTIPLE MYELOMA

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Multiple myeloma as a disease entity presents marked variations in its clinical manifestations. Until recently the diagnosis of this disease during life was a comparatively infrequent occurrence. The condition was suspected only in cases in which bone tumors had developed or in which well defined radiographic changes were observed. In rare instances it was discovered accidently, in connection with certain operations—following laminectomy (Christian (9)) or after resection of clavicle (Bloodgood (6)). Cases have been occasionally diagnosed during life through the finding of Bence-Jones' protein in the urine, but confirmation of the diagnosis could not be obtained until a post mortem examination was undertaken. There is little doubt that many cases have been missed because of failure to obtain a post mortem examination or, during life, to obtain bone marrow by means of biopsy or sternal puncture.

The importance of the latter procedure is well illustrated by the marked increase in the number of cases reported in the past two years. Only sixty-six genuine cases were collected from the literature by Wallgren (35) for the years 1873 to 1920, and 425 cases by Geschickter and Copeland (13) 1848 to 1928 (including thirteen cases of their own observed at Johns Hopkins Hospital from 1906 to 1928). At The Mount Sinai Hospital only three cases were observed from 1916 to 1935. This is in strong contrast to the thirteen cases observed at this hospital during the past two and one-half years—all of which were diagnosed by means of sternal puncture. In two of the cases, biopsy of the sternum was also performed, and additional confirmation by post mortem examination was obtained in the majority of cases. The report of these recent cases forms the basis of the present article.

The use of sternal puncture as a routine procedure in the study of obscure anemias and cases presenting skeletal changes has gradually led to its introduction as a diagnostic method in multiple myeloma. The finding of myeloma cells in the marrow served as a basis for continued study of the blood and urine, in addition to roentgen examination of patients in whom the disease was not suspected. On the other hand, the absence of myeloma cells in the bone marrow of suspected cases served to rule out this condition.

CASE REPORTS

Group A: Patients Showing Bence-Jones' Proteinuria

Case 1. History A Jewish man, forty-eight years of age, was admitted to the Consultation Service, December 30, 1935, with a history, covering a period of two years, of pain in the lumbosacral region extending up to the cervical region. The pain had been somewhat relieved following the use of a support. The patient appeared to be well nourished. He walked slowly. The spine remained rigid on movement or in an attempt to bend. There was slight tenderness on heavy percussion of the lumbar spine.

Laboratory Data. The urine showed the presence of Bence-Jones' protein; 3 plus albumin; and 1.024 specific gravity. The blood count was as follows: hemoglobin, 80 per cent; red cells, 4,520,000; white cells, 9,200; platelets, 190,000; nonsegmented neutrophiles, 1 per cent; segmented neutrophiles, 58 per cent; eosinophiles, 3 per cent; lymphocytes, 38 per cent; monocytes, 2 per cent. The blood proteins (Table I) were: albumin, 5.7 per cent; globulin, 2.1 per cent. X-ray examination showed areas of rarefaction of pelvic bones, proximal fourth of both femora, and frontal bone. Signs of compression were observed in a few of the lumbar vertebrae. There was mottling of the third and fourth ribs and fracture of the third right rib.

Sternal puncture (Table II) revealed 18.5 per cent plasma cells.

Course. The patient developed progressive asthenia, fluid in the pleural cavity, and intestinal bleeding terminally. He died at his home in September, 1937.

Case 2. History (Adm. 389665). A female, thirty-eight years old, was admitted to the Consultation Service, October 23, 1935, with a history of attacks of pain on the right side, covering a period of eleven years. The patient had been operated upon for gall-bladder disease six years previously with some relief from pain for a few years. In addition to these attacks, the patient developed edema of the ankles. Physical examination was essentially negative at this time.

Laboratory Data (Consultation Clinic). The blood picture was as follows: hemoglobin, 65 per cent; red cells, 3,580,000; white cells, 5,300; nonsegmented neutrophiles, 5 per cent; segmented neutrophiles, 34 per cent; eosinophiles, 1 per cent; basophiles, 1 per cent; lymphocytes, 58 per cent; monocytes, 1 per cent. The blood chemistry showed the following: cholesterol, 270 mgm.; cholesterol ester, 90 mgm.; urea nitrogen, 15 mgm.; albumin, 4.8 per cent; globulin, 2.1 per cent. The urine showed an occasional white blood cell; a rare hyaline cast; albumin, 4 plus; concentration, 1.030. X-ray examinations at this time revealed evidence of productive spondylitis; and some arthritic changes were noted in both sacro-iliac synchondroses.

Because of continued pain on the right side and the development of generalized bone pains, the patient was admitted to the Semi-Private Pavilion on February 6, 1936. Physical examination was negative, except for generalized bony tenderness.

Laboratory Data (Hospital). X-ray examinations showed multiple rarefaction of the ribs and skull. Urine now showed Bence-Jones' protein. The blood picture was: hemoglobin, 56 per cent; red cells, 3,100,000; white cells, 4,100; platelets, 120,000; nonsegmented neutrophiles, 6 per cent; segmented neutrophiles, 41 per cent; lymphocytes, 50 per cent; myelocytes, 1 per cent; monocytes, 1 per cent. Of note are the thrombocytopenia and, as in the previous blood count, the hypochromic anemia and lymphocytosis.

Sternal puncture revealed a hypoplastic marrow with an increase in plasma cells (17 per cent).

Course. The patient received Coley's serum and transfusions, followed by radiotherapy to the bones. The anemia became more marked and a moderate number of myelocytes and myeloblasts appeared in the blood. The patient died of progressive asthenia. Permission for a post mortem examination could not be obtained.

Case 3. History (Adm. 393832). A male, fifty-one years old, was first admitted to the Consultation Service, January 1, 1936, with a history of backache for three months. Soon thereafter he developed pain in the lower ribs on both sides. Physical examination at this time revealed a well developed and well nourished male who held his back rigid on walking. The blood pressure was 128 systolic and 86 diastolic.

TABLE I

Essential blood chemistry, Bence-Jones' proteinuria and X-ray findings

| Case No. | Chemistry | | | | | | | | X-ray |
	Albumin	Globulin	Formol gel	Calcium	Phosphorus	Phosphatase units	Fibrinogen	Bence-Jones protein	
1	5.7	2.1	—	—	—	—	—	Pos.	Pos.
2	4.7	3.08	—	—	—	—	264	"	"
3	2.7	2.7	—	8.5	3.5	—	—	"	"
4	3.3	5.5	Pos.	—	—	—	—	"	"
5	3.9	24	—	14.8	4.0	20.0	410	Neg.	"
6	3.0	6.4	Pos.	—	—	—	—	"	"
7	3.7	2.8	Neg.	—	—	—	—	"	"
8	5.4	2.7	—	12.5	7.5	10.0	—	"	"
9	3.1	6.3	—	—	—	—	—	"	"
10	4.3	2.6	Neg.	—	—	—	—	"+	"
11	5.6	2.1	"	—	—	—	—	"	"
12	2.2	6.5	Pos.	13.4	3.6	4.7	—	"	"
13	2.7	4.8	"	9.3	4.4	9.7	115	Pos.	"

+ *Positive terminally*

Laboratory Data (Consultation Clinic). The blood count was as follows: hemoglobin, 84 per cent; red cells, 4,450,000; white cells, 8,200; platelets, 210,000; nonsegmented neutrophiles, 2 per cent; segmented neutrophiles, 60 per cent; lymphocytes, 33 per cent; monocytes, 5 per cent. The urine showed 2 plus albumin; a few hyaline casts; calcium oxalate crystals; a few epithelial cells; and specific gravity of 1.024; it was positive for Bence-Jones' protein. X-ray examinations revealed changes in the pelvis, compatible with multiple myeloma.

Sternal puncture showed the presence of numerous myeloma cells (20 per cent). Radiotherapy over a period of four months seemed to aggravate the symptoms.

On May 29, 1936, the patient was admitted to the service of Dr. B. S. Oppenheimer. Three weeks prior to his entry he had developed a sore throat and cough; in addition, he had lost considerable weight and was markedly weak. The day before admission

TABLE II

Case No.	Sex	Age in years	Sternal marrow differential												
			Myeloblasts	Myelocytes	Non-segmented neutrophils	Segmented neutrophils	Eosinophilic myelocytes	Eosinophils	Basophils	Lymphocytes	Hematogones	Plasma myeloma cells	Reticulum cells	Megakaryocytes	Nucleated red cells
1	♂	48	0.2	7.2	17.0	33.3	0.9	1.5	—	—	—	18.5	—	0.4	21.0
2	♀	38	1.6	10.0	4.0	32.0	—	1.4	—	23.0	3.0	17.0	—	—	8.0
3	♂	51	0.2	1.6	4.0	24.0	0.4	1.6	—	44.2	—	20.0	—	—	4.0
4	♀	62	2.0	13.2	11.2	8.0	0.8	1.4	—	1.4	1.6	30.4	2.2	0.4	27.4
5	♂	46	5.0	3.0	6.0	65.6	0.2	3.0	—	10.0	—	5.0	—	—	2.2
6	♂	55	1.4	14.2	20.8	13.8	0.8	—	—	0.8	1.6	26.4	1.8	0.2	18.2
7†	♀	60	2.4	30.4	25.0	15.0	0.4	0.4	0.4	4.8	1.4	3.6	1.2	—	15.0
8	♂	59	1.3	8.3	4.6	18.6	0.3	2.0	—	1.3	—	33.0	2.6	0.3	27.7
9†*	♂	56										Many			
10	♀	55	5.5	21.5	5.5	2.7	1.1	0.4	—	4.3	—	9.2	2.7	—	46.6
11	♂	50	3.5	26.4	14.9	13.3	0.7	0.2	0.6	2.2	6.5	20.3	0.3	—	10.7
12	♂	57	1.2	3.2	3.2	11.0	0.2	0.6	—	6.0	5.0	65.0	1.2	—	3.0
13	♀	60	1.5	30.5	25.1	21.7	—	0.1	—	—	0.8	3.0	—	—	17.3

† Biopsy (sternal) also done
* Exact figures not available

he developed chills and fever. Physical examination at this time revealed a pale, febrile man with signs of consolidation at both bases. The liver edge was felt two fingers' breadth below the costal margin. There was kyphoscoliosis of the thoracic spine.

Laboratory Data (Hospital). The blood count at this time was: hemoglobin, 36 per cent; red cells, 1,860,000; white cells, 1,500; platelets, 90,000; nonsegmented neu-

trophiles, 21 per cent; segmented neutrophiles, 46 per cent; myelocytes, 1 per cent; lymphocytes, 30 per cent; monocytes, 2 per cent. There was a marked depression of all the elements. The blood chemistry was: serum globulin, 2.7 per cent; serum albumin, 2.7 per cent; calcium, 8.5 mgm.; phosphorus, 3.5 mgm. The Takata-Ara reaction was 3 plus.

Sternal puncture at this time again showed the presence of about 20 per cent plasma cells, typical of multiple myeloma. X-ray examination revealed areas of rarefaction of the dorsal spine, the ribs, and scapulae.

Course. The patient became progressively weaker, and died eight days after admission. Post mortem findings confirmed the diagnosis of multiple myeloma.

Case 4. History (Adm. 397917). A female Hungarian cook, sixty-two years of age, was admitted to the medical service of Dr. B. S. Oppenheimer, September 2, 1936, with a history of headache for four years, frequent epistaxis for two years, and numbness, pain and paresthesia of the left big toe, with shooting pains down the left lower extremity for one year. The patient had lost fifty pounds in weight. Physical examination revealed a chronically ill woman with uremic breath and puffy eyelids; there was moderate kyphosis. Diffuse hyperesthesia was present. The blood pressure was 190 systolic and 110 diastolic.

Laboratory Data. The blood count was: hemoglobin, 52 per cent; red cells, 3,570,000; white cells, 13,700; platelets, 70,000; normoblasts, 1 per 100 white cells; reticulocytes, less than 0.5 per cent; nonsegmented neutrophiles, 13 per cent; segmented neutrophiles, 54 per cent; eosinophiles, 3 per cent; lymphocytes, 22 per cent; monocytes, 8 per cent. The blood picture showed a hypochromic anemia and a thrombocytopenia. The Congo-red test showed 40 per cent retention in one hour. The blood chemistry was albumin, 3.3 per cent; globulin, 5.5 per cent; total protein, 8.8 per cent; urea nitrogen, 40 mgm.; chlorides, 420 mgm.; creatinin, 4.5 mgm. Formol-gel reaction was positive. The urine had a fixed specific gravity, 1.010; 3 plus albumin; Bence-Jones' protein was present. X-ray examination showed mottling of the skull.

Sternal puncture revealed marked increase in plasma cells, indicating the presence of multiple myeloma.

Course. The patient was given X-ray treatment but failed to respond; she died one month after admission to the hospital. Post mortem examination confirmed the diagnosis of multiple myeloma.

Group B: Albuminuria with Absence of Bence-Jones' Protein

Case 5. History (Adm. 386668). A male, Russian Jew, forty-six years of age, was admitted to the medical service of Dr. George Bachr, November 12, 1935, with a history of bronchitis and expectoration for many years. Three months prior to admission the patient suddenly developed pain in the entire left lower extremity, lasting one and one-half months and then subsiding. Following this he had an episode of sharp stabbing pain in the left chest and, while bending over, felt one of his ribs crack. About three weeks before admission he developed a lump over the left clavicle; it was not tender but seemed to increase in size.

Examination. The patient was a well developed and moderately obese, plethoric man with a soft, bean-sized nodule over the left occipital region, and a few discrete nodes of the same dimensions in the lateral cervical region. Fulness and swelling were present over the left sternoclavicular and infraclavicular regions, and moderate swelling over the tenth and eleventh ribs, with exquisite tenderness over these regions. The liver edge was felt below the costal margin. There were bilateral inguinal herniae. Tenderness was noted on percussion over the twelfth dorsal and upper lumbar vertebrae.

Laboratory Data. The blood picture was: hemoglobin, 76 per cent; red cells, 4,200,000; white cells, 9,000; platelets, 240,000; nonsegmented neutrophiles, 15 per cent; segmented neutrophiles, 46 per cent; myelocytes, 1 per cent; myeloblasts, 3 per cent; lymphocytes, 20 per cent; plasma cells, 4 per cent; monocytes, 1 per cent. There was a slight increase of immature myeloid and plasma cells. The blood chemistry was: urea nitrogen, 16 mgm.; sugar, 105 mgm.; calcium, 14.8 mgm.; phosphorus, 4 mgm.; albumin, 3.9 per cent; globulin 2.4 per cent; total protein, 6.2 per cent; fibrinogen, 0.410 per cent; phosphatase 20 King-Armstrong Units; Wassermann negative; Congo-red test showed 30 per cent absorption in one hour. The urine contained 2 plus albumin; Bence-Jones' protein was not present. Biopsy of the tumor of the scalp was reported by Dr. Klemperer as showing lymphoblastic myeloma. X-ray examinations revealed thickening of the pleura. There were a few areas of rarefaction in the medial portion of the left clavicle, and irregular areas of rarefaction scattered throughout the entire skull, involving the jaw.

Sternal puncture revealed a markedly cellular marrow with a pronounced increase in segmented neutrophiles and scattered clumps of the typical myeloma cells.

Course. Radiotherapy was administered, but the patient went progressively down hill and died ten days after admission. Post mortem examination confirmed the diagnosis.

Case 6. History (Adm. 400298). A male, fifty-five years of age, was admitted to the service of Dr. B. S. Oppenheimer, October 27, 1936, with a history of a chancre forty years previously. He was in good health until four weeks before admission, when epistaxis began. These attacks continued in spite of local treatment, and the patient became very weak.

Examination. The patient was a well developed, anemic, middle-aged man. Blood clots were present in the nose. The liver was felt three fingers' breadth below the costal margin. The blood pressure was 186 systolic and 120 diastolic.

Laboratory Data. The blood count was hemoglobin, 36 per cent; red cells, 2,140,000; white cells, 5,350; platelets, 30,000; nonsegmented neutrophiles, 7 per cent; segmented neutrophiles, 61 per cent; eosinophiles, 3 per cent; lymphocytes, 21 per cent; monocytes, 8 per cent. The blood picture showed a marked anemia and thrombocytopenia suggestive of purpura hemorrhagica. The bleeding time was four minutes; coagulation time, seven minutes; tourniquet test was slightly positive; there was no clot retraction. The urine showed 3 plus albumin, a specific gravity of 1.008–1.022; but was negative for Bence-Jones' protein. The blood chemistry was: urea nitrogen, 31 mgm.; albumin, 3 per cent; globulin, 6.4 per cent. Formol-gel reaction was positive. X-ray examination of the chest revealed a pathological fracture of the eighth rib. The skull showed a small area of rarefaction in the left frontal region.

Sternal puncture (Figure 1) revealed typical plasma cells of multiple myeloma (26 per cent).

Course. A transfusion and some radiotherapy were administered and the patient left the hospital under the care of his physician. He remained in poor health, complaining of weakness and discharge from the ears. On January 18, 1937 he had a recurrence of the epistaxis and was admitted to Lincoln Hospital, where he died fourteen days after admission. The diagnosis of multiple myeloma was confirmed by post mortem examination.

Case 7. History (Adm. 404718). A female, sixty years old, was admitted to the service of Dr. George Baehr, February 16, 1937, with a one-year history of severe upper right quadrant pain radiating to the back; there were also fleeting but sharp pains in the region of the lower back, making sitting extremely painful and difficult. The patient was feverish during the attacks (of which there were ten). Residual soreness and pain were present in the lower back during the free intervals. There

were also episodes of pain, sticking in nature, below the left breast. Her past history included a cholecystectomy performed ten years prior to the present admission, for recurrent biliary colic.

Examination. The patient was a well developed, very obese woman, appearing acutely ill. There were a few scattered linear hemorrhages in both fundi, with a white exudate on the right. Marked tenderness was noted in the right upper quadrant. There were a few crepitant râles at the left base. The blood pressure was 130 systolic and 70 diastolic.
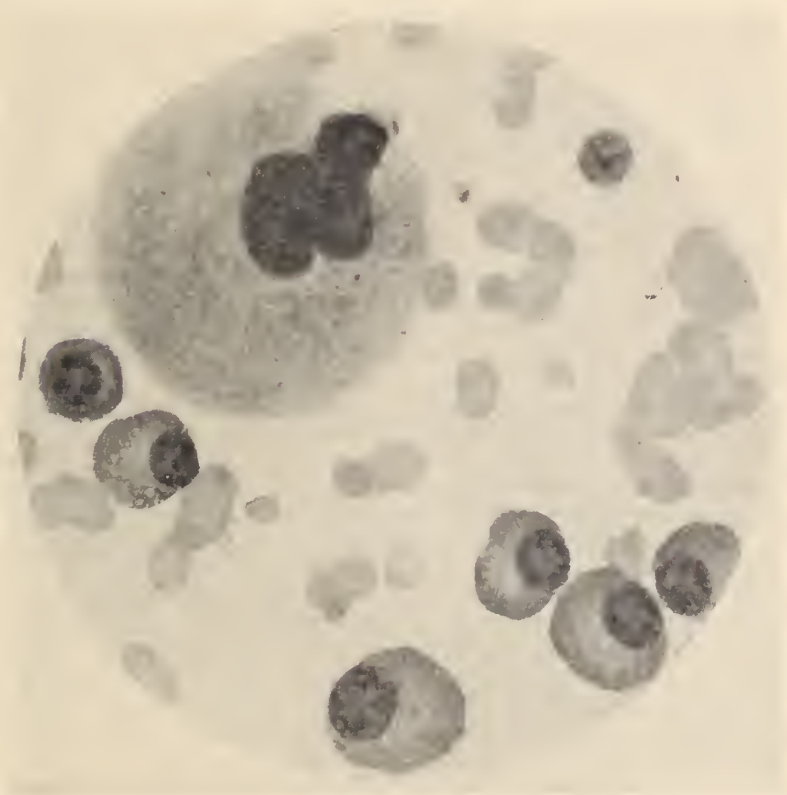
Fig. 1 (Case 6). Sternal Bone Marrow. Megakaryocyte and plasma (myeloma) cells, some finely vacuolated. (× 800).

Laboratory Data. The blood count was: hemoglobin, 72 per cent; red cells, 3,960,000; white cells, 9,200; platelets, 170,000; nonsegmented neutrophiles, 1 per cent; segmented neutrophiles, 58 per cent; lymphocytes, 35 per cent; monocytes, 6 per cent. The urine showed a specific gravity of 1.020; albumin, 2 plus; but was negative for Bence-Jones' protein. The blood chemistry was albumin, 3.7 per cent; globulin, 2.8 per cent; total protein, 6.5 per cent. Blood Wassermann test was negative. An electrocardiogram showed evidence of myocardial damage. X-ray examination of the dorsolumbar spine revealed partial destruction of the body of the third lumbar vertebra with compression. The entire anterior third of the body was rarefied. There were similar lesions in the sixth and seventh ribs on the left side. X-ray examinations of the skull, knees, and elbows showed rarefaction.

Sternal puncture revealed an increase in plasma cells (3.6 per cent) suggesting multiple myeloma, but it was deemed advisable to have a sternal biopsy performed. Dr. Klemperer considered the biopsy suggestive of multiple myeloma. Smears of this biopsy showed the presence of clumps of myeloma cells.

Course. Radiotherapy was begun and the patient was discharged under the care of her physician.

Case 8. History (Adm. 410336). A German tailor, fifty-nine years of age, was admitted to the service of Dr. George Baehr on June 19, 1937, with a history of pleuritic pain in the left lower chest, for a period of nine weeks. His previous history included a mastoidectomy twenty-eight years ago, a concussion of the brain nine years ago, pleurisy twice (six years and one year ago), and lumbar pain twice (nine years and five years ago). A lump on the scalp had been noted for one year. The recent illness began nine weeks before admission to the hospital, with pain in the left chest, aggravated on respiration. The patient's physician diagnosed the condition as pleurisy. Three weeks after the onset, the patient had an episode of vomiting which lasted one week. During the three weeks prior to admission, he had pain in the right and, to a lesser degree, in the left loin; this was associated with albuminuria and hematuria. He had lost thirty-eight pounds since the onset of his recent illness.

Examination. The patient was a well-developed and well-nourished man, pale and apparently chronically ill. A large mass was present over the left parietal region of the skull. Both disks were blurred; there were fine crackling râles at both bases. The heart was slightly enlarged. The blood pressure was 140 systolic and 80 diastolic. There was percussion tenderness over the first lumbar spine.

Laboratory Data. Blood chemistry was: phosphorus, 7.5 mgm.; calcium, 12.5 mgm.; phosphatase, 10 King-Armstrong Units; Takata-Ara, negative; urea nitrogen, 78 mgm.; carbon dioxide, 45 vol. per cent; albumin, 5.4; globulin, 2.7. Congo-red test showed 32 per cent tissue absorption in one hour. The urine showed a specific gravity of 1.012; albumin, 2 to 3 plus; there were occasional granular casts, a few red blood cells and white blood cells; Bence-Jones' protein negative. Blood count was hemoglobin, 42 per cent; red cells, 2,390,000; white cells, 7,450; platelets, 230,000; nonsegmented neutrophiles, 9 per cent; segmented neutrophiles, 70 per cent; eosinophiles, 2 per cent; basophiles, 1 per cent; lymphocytes, 16 per cent; monocytes, 2 per cent. The blood picture was that of a marked anemia. X-ray examination of the skull showed destructive areas, circular in appearance, and of varying size. Similar changes were found in the mandible and fifth left rib. There was compression of the twelfth dorsal and fourth lumbar vertebrae.

Sternal puncture revealed numerous myeloma cells (33 per cent).

Course. In the presence of bilateral papilledema, mottling of the bones of the skeleton, anemia, pleuritic and renal pain, hematuria, azotemia, and the mass over the left parietal region, a metastatic type of malignancy was believed to be present, probably hypernephroma. Multiple myeloma was not suspected, because of the absence of Bence-Jones' protein, and only by means of sternal puncture was an absolute diagnosis made.

Radiotherapy was administered, but the patient became weaker and more drowsy. His temperature fluctuated up to 101°F. His family believed he could be taken care of at home, and he was discharged and placed under the care of his physician.

Case 9. History (Adm. 380126). A British Colony negro, fifty-six years of age, had been well until six months before admission (May 22, 1935) when he developed pain in both sacro-iliac regions, and four months later, following an injury to the chest, he noted a plum-sized mass over the sternum.

Examination. The patient was a well developed, emaciated negro, who complained of pain in the spine when moving about. There was an egg-sized tender swelling in the midsternum at the level of the second rib. The prostate was moderately enlarged and somewhat nodular.

Laboratory Data. The blood count was hemoglobin, 66 per cent; red cells, 3,380,000; white cells, 6,400; platelets, 320,000; non-segmented neutrophiles, 14 per cent; segmented neutrophiles, 59 per cent; lymphocytes, 21 per cent; plasma cells, 1 per cent; monocytes, 6 per cent. Except for a hypochromic anemia the blood picture was normal. Blood Kahn test was negative. Urine was negative for Bence-Jones' protein; there was persistent albuminuria with high specific gravity to 1.034. The blood chemistry was: total protein, 9.4 per cent; albumin, 3.1 per cent; globulin, 6.3 per cent. X-ray examination showed marked compression of all vertebral bodies, particularly those in the lower lumbar region; diminished density was scattered throughout both clavicles and skull.

Sternal puncture revealed many myeloma cells. Sternal biopsy was reported by Dr. Klemperer as plasma cell myeloma.

Course. Although the patient was given a transfusion, in addition to supportive medication, he died on June 6, 1935. Post mortem examination confirmed the diagnosis of multiple myeloma involving all the bones examined; there was also plasma cell infiltration of the lymph nodes.

Case 10. History. (Adm. 404701). A woman, fifty-five years old, was first admitted January 29, 1937, to the Consultation Service because of weakness and pallor of three months' duration. One month prior to admission she developed aches throughout the body and pain in the right shoulder; there was also dyspnea and swelling of the abdomen.

Examination. She was a well developed, pale, chronically ill woman. The heart was enlarged to the left. The liver was enlarged a hand's breadth below the costal margin; evidence of ascites was present. The blood pressure was 148 systolic and 98 diastolic.

Laboratory Data. (Consultation Clinic). The blood count was: hemoglobin, 36 per cent; red cells, 2,050,000; white cells, 5,100; platelets, 240,000; reticulocytes, 0.3 per cent; nonsegmented neutrophiles, 5 per cent; segmented neutrophiles, 49 per cent; eosinophiles, 1 per cent; myelocytes, 3 per cent; myeloblasts, 3 per cent; lymphocytes, 29 per cent; monocytes, 10 per cent. The blood picture showed a hyperchromic anemia and definite increase in immature myeloid cells; these findings were suggestive of bone marrow irritation, or possibly, leukopenic myeloid leukemia. The urine had a specific gravity of 1.014; 3 plus albumin; epithelial cells and a few clumps of white cells; it was negative for Bence-Jones' protein. Blood urea nitrogen was 28 mgm.; blood Kahn test was negative. Sedimentation rate was 20 minutes.

Sternal puncture revealed 17 per cent plasma cells which led to the diagnosis of myeloma.

Because of increasing weakness, the patient was admitted to the medical service of Dr. George Baehr, February 16, 1937.

At this time she appeared a pale, chronically ill woman showing signs of recent loss in weight. The heart was moderately enlarged to the left, with a systolic murmur at the left border. The spleen and liver were still moderately enlarged.

Laboratory Data. (Hospital): The blood count was: hemoglobin, 49 per cent; red cells, 1,940,000; white cells, 9,800; platelets, 160,000; nonsegmented neutrophiles, 6 per cent; segmented neutrophiles, 38 per cent; eosinophiles, 3 per cent; basophiles, 1 per cent; myelocytes, 3 per cent; myeloblasts, 8 per cent; lymphocytes, 30 per cent; plasma cells, 2 per cent, monocytes, 11 per cent, reticulocytes, 0.5 per cent. At this time there was a hyperchromic anemia with a few immature myeloid cells. Total blood protein was 6.9 per cent; albumin, 4.3 per cent and globulin, 2.6 per cent. The urine contained 4 plus albumin; specific gravity, 1.016; it was negative for Bence-Jones' protein. X-ray examination revealed moderate osteoporosis of the ribs.

Sternal puncture again showed a marked increase in plasma cells in the bone marrow, characteristic of multiple myeloma. The patient was discharged and placed

under the care of a private physician, but was readmitted two days later for cardiac failure. Bence-Jones' protein was discovered for the first time. The patient died. Permission for a post mortem examination could not be obtained.

Case 11. History. A Russian salesman, fifty years of age, was admitted to the Consultation Service, October 4, 1937, with a history of dull pain in the lower cervical region for three to four years. During the four months prior to admission the pain had become more frequent and severe and was accompanied by knife-like shooting pains radiating across both shoulder regions. In addition, during the past five to six weeks, pain was felt in both left and right chest regions anteriorly, more or less

FIG. 2 (Case 11). Osteoporosis and compression of sixth cervical vertebra

constantly, but aggravated by raising the left arm. The patient had had a chronic post-nasal discharge for many years.

Examination. The patient was a well developed and well nourished man, with an area of hyperesthesia over both shoulder girdles, anteriorly and posteriorly. The blood pressure was 110 systolic, and 78 diastolic. A diagnosis of cervical spondylitis was made.

Laboratory Data. The blood count on October 29, 1937 was: hemoglobin, 94 per cent; red cells, 4,810,000; white cells, 6,200; platelets, 170,000; nonsegmented neutrophiles, 1 per cent; segmented neutrophiles, 54.5 per cent; eosinophiles 0.5 per cent; myelocytes, 0.5 per cent; lymphocytes, 40 per cent; monocytes, 3.5 per cent. The

urine examination was negative.   The blood chemistry was: albumin, 5.6 per cent;
globulin, 2.1 per cent; formol-gel reaction was negative.   X-ray examination showed
osteoporosis and compression of the sixth cervical vertebra (Figure 2).   In the skull
a large area of rarefaction was disclosed in the parietal region.   Two smaller areas
of rarefaction were seen in the shaft of the humerus.

Sternal puncture revealed 20.3 per cent plasma myeloma cells.

Radiotherapy was advised and the patient was discharged under the care of his
private physician.   He is still under observation.
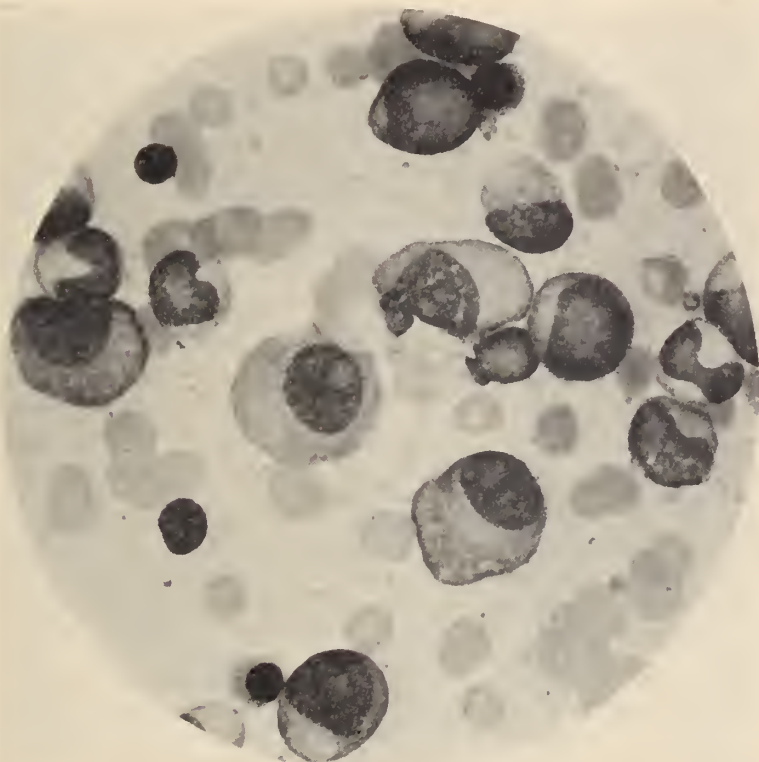
FIG. 3 (Case 12).   Sternal Bone Marrow.   Myeloma and immature leucoblastic
cells, all with eccentric nuclei.   Note the large nucleoli in the myeloma cells.   ($\times$ 800)

Case 12.   History. (Adm. 413546).   A man fifty-seven years old, was first ad-
mitted to the Consultation Service, August 9, 1937, because of severe pain in the lower
right axilla of several days' duration.   During the study of the case, his general
condition became so poor that he was transferred to the Semi-Private Pavilion where
additional studies were undertaken.

A rapid sedimentation time was present at that time and X-ray findings were
suggestive of osteo-arthritis; but this did not adequately explain his symptoms.   A
metastatic malignancy was believed to be present at this time, but the patient left
the hospital before studies could be completed.

Laboratory Data. (Consultation Service).   Hemoglobin was 75 per cent; red

cells, 3,980,000; white cells 8,100; segmented neutrophiles, 53 per cent; eosinophiles, 1 per cent; lymphocytes, 45 per cent; monocytes, 1 per cent. The urine showed a faint trace of albumin. The spinal fluid showed a positive Pandy reaction.

The patient was readmitted to the Semi-Private Pavilion, November 17, 1937, as symptoms continued, with more pronounced pain in the left hip and shoulder, weakness and anemia.

Examination. The patient was a well nourished, obese man with marked pallor. There was bony tenderness and pain on motion; otherwise the examination was negative.

Laboratory Data. (Hospital). The blood examination showed hemoglobin, 48 per cent; red cells, 2,620,000; white cells, 8,250; platelets, 240,000; nonsegmented neutrophiles, 6 per cent; segmented neutrophiles, 62 per cent; segmented eosino-philes, 1 per cent; lymphocytes, 19 per cent; monocytes, 11 per cent; myeloblasts, 1 per cent; reticulocytes, 0.5 per cent. The blood picture at this time showed a marked anemia but was otherwise normal. Blood chemistry was: albumin, 2.2 per cent; globulin, 6.5 per cent; calcium, 13.4 mgm. per 100 c.c.; phosphorus, 3.6 mgm.; phosphatase, 4.7 King-Armstrong units; Formol-gel reaction, positive; Takata-Ara reaction, strongly positive. The urine showed a faint trace of albumin but was negative for Bence-Jones' protein. Microscopic examination showed occasional red cells; an occasional hyaline cast and some white cells. X-ray studies at this time showed areas of destruction in the ribs, skull, humeri, pelvis and lumbar spine.

Sternal puncture revealed a marked increase in plasma cells (65 per cent) (Figure 3). The nuclei showed the presence of a larger nucleolus and a light perinuclear zone in some cells.

The patient is receiving liver extract intramuscularly and is still under observation.

Group C: Myelocytic Myeloma

Case 13. History (Adm. 393767). A Palestinian housewife, sixty years of age, was admitted for the first time, May 27, 1936, with a history of loss in weight and pallor over a period of five months. One month prior to admission she developed a sore throat followed by weakness, dyspnea, ill-defined chest and back pain, severe pallor, anorexia, and insomnia. Her past history included malarial attacks until thirty years ago, and asthma for the past thirty years.

Examination. The patient was a pale, obese woman with moderate dyspnea. Signs of fluid were present in the right chest. The liver was enlarged to the iliac crest. The spleen was palpable three fingers' breadth below the costal margin. There was pitting edema of the feet, ankles and pretibial areas. The blood pressure was 150 systolic and 80 diastolic.

Laboratory Data. The blood picture was: hemoglobin, 47 per cent; red cells, 3,750,000; white cells, 48,000; platelets, 60,000; reticulocytes, 4.3 per cent; nonseg-mented neutrophiles, 9 per cent; segmented neutrophiles, 66 per cent; lymphocytes, 7 per cent; monocytes, 6 per cent; myelocytes, 8 per cent; myeloblasts, 4 per cent. There was a marked anemia leucocytosis, thrombopenia with the presence of imma-ture cells. The blood Wassermann test was negative. Blood chemistry was: urea nitrogen, 39 mgm.; sugar, 158 mgm.; cholesterol, 140 mgm.; cholesterol ester, 20 mgm.; albumin, 2.7 per cent; globulin, 4.8 per cent; total protein, 7.5 per cent; Takata-Ara reaction, 4 plus; Formol-gel reaction, positive. X-ray examination of the chest showed an effusion of the right pleural cavity; healed fractures of the fifth and sixth ribs on the right side posteriorly. X-ray examination of the long bones showed osteoporosis.

Sternal puncture revealed a very cellular marrow with a marked increase of myelo-cytes with eccentric nuclei. The plasma cells were increased to 3 per cent.

Course. The patient was given three transfusions and discharged. She was readmitted, August 4, 1936. She had not been well since her discharge; the anemia became progressive and there was a recurrence of symptoms.

The blood count was essentially the same except for a more marked anemia (hemoglobin, 39 per cent).

The patient was given a transfusion and referred to the Hematology Clinic where she received mercupurin and liver extract. She is still under observation.

A second bone marrow aspiration on November 3, 1937, showed a picture similar to that described above. Bence-Jones' protein was found to be present at this time.
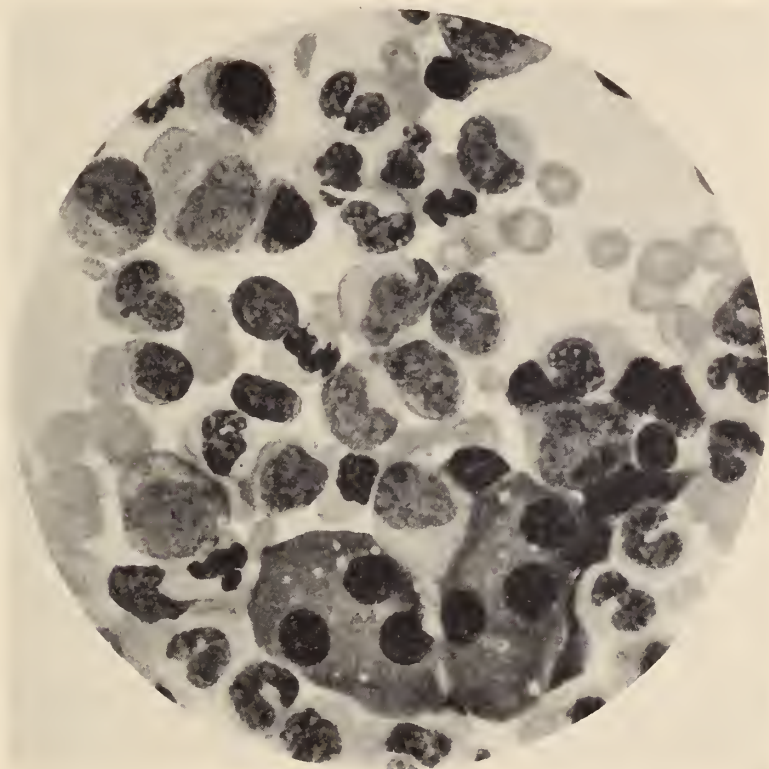
FIG. 4 (Case 13). Sternal Bone Marrow Smear of Myelocytic Myeloma. Two multinuclear myeloma cells and numerous myelocytes with eccentric nuclei, many non-segmented and segmented neutrophiles. (× 800).

X-ray picture, November 15, 1937, showed small areas of rarefaction in the humerus, pelvis, femur, and vertebrae.

DISCUSSION

Clinical Picture. Patients in this series showed marked variation in symptoms. Characteristic pains in the back or chest were present in some cases, generalized bone pains occurred in others, and in one patient (Case 11), pain in the back of the neck was present for four years. Weak-

ness and pallor constituted the outstanding manifestation in two instances (Cases 10 and 13) and epistaxis (Case 6) was the chief symptom which brought the patient to the hospital in another case. Without the aid of the sternal puncture and the X-ray examinations in these three cases, attention would probably have been focussed upon the anemic or throbocytopenic phase, and the underlying bone involvement might have been overlooked. This applies also in the other cases with bone pains, the condition being at first regarded as spondylitis or radiculitis. Roentgenologic examination proved instrumental in directing attention to a metastatic rather than to a generalized skeletal involvement and, finally, in all cases except those with Bence-Jones' proteinuria, the correct diagnosis would not have been possible without sternal puncture; nor would the objective findings, in all except two cases, have led one to suspect myelomatosis. The physical examination in some instances was practically negative; in others, spondylitis was suggested on the basis of stiffness of the spine and difficulty in bending and in picking up objects. Definite nodules were present in only two cases, in the sternum of Case 9 and the skull of Case 8.

Blood Picture. The blood picture in multiple myeloma is not characteristic; it may, in fact, be normal. Usually there is an anemia of the hypochromic type; occasionally, it may be hyperchromic (Case 10), as reported by Goadby (15), Varadi (33). The white cells also show variation—leucopenia to leucocytosis—and the differential count is not characteristic. There may be slight lymphocytosis (Case 2), slight increase of plasma cells or myelocytes and myeloblasts. The finding of myeloblasts (Cases 5, 10 and 13) is strongly suggestive of leukemia, as noted by Krumbhaar (23). In a case of myelocytic myeloma (Case 13), the blood picture was indistinguishable from leucopenic myeloid leukemia.

The platelets were normal in the greater number of our cases. Varadi reports normal platelet counts in five cases. There was a marked and persistent thrombocytopenia in five of our series, but this was not associated with purpura. In one case there were severe nosebleeds, which might be attributed to a diminution in the number of platelets.

Blood Proteins and Calcium (Table I). Hyperproteinemia (Jacobson (18)) is considered one of the chief suggestive characteristics of this disease. Its mechanism, however, is not understood. According to Bing (3), it is apparently associated with an increase in plasma cells in the marrow of myelomatosis and other conditions. Perlzweig, Delrue and Geschickter (27), Reimann (28), Foord (12), Jeghers and Selesnick (19) and others found a marked increase in the globulin fraction which may be accompanied by a positive formol-gel reaction, as pointed out by Bing (4), and Wise and Gutman (36). The latter found a positive reaction in five cases of myeloma associated with a hyperglobulinemia and a negative formol-gel reaction in two cases with a normal serum globulin. In

our series of thirteen cases, hyperproteinemia was present in only six. The formol-gel reaction was positive in the four in which it was done. Rouleaux formation of the red cells was also present in these cases (Figure 1); this may be due to the increased fibrinogen, as reported by Reimann, Foord, and Sweigert (32).

Gros (16) and Jeghers (20) have found markedly positive Takata-Ara reactions. The Takata-Ara reaction was positive in Cases 3, 11 and 13 of our series.

The serum calcium may be increased (Cases 5, 8 and 12) and may be associated with skeletal rarefaction. The calcium may be transported to other organs, where it is deposited. Hypercalcemia was also found in the cases reported by Foord, Shirer, Duncan and Haden (31), Jores (21), Reimann and Sweigert. Blatherwick (5) studied calcium metabolism in a case of myelomatosis and was unable to find a positive calcium balance.

Hyperproteinemia and hypercalcemia must be regarded as sugggestive findings (Gutman (17)), but the presence of normal amounts of serum proteins (Chester (8)), and calcium is not infrequent in multiple myeloma.

Urinary Findings (Table I). The presence of nephritis or its characteristic nephropathy (Bell (2)) is not unusual in multiple myeloma. Albumin was found in all of our cases except one, and casts were often present in the urine.

The presence of the Bence-Jones' protein in the urine was discovered in 1847, many years before the disease, multiple myeloma, was identified by von Rustizky (29) in 1873. Sixteen years later, Kahler (22) found Bence-Jones' proteinuria in a case of multiple myeloma. Bence-Jones' proteinuria was not a frequent finding in our series; it was present in only five instances. It was also observed in one of our cases of myelocytic myeloma. This protein was found only just before death in Case 10.

X-ray Findings. X-ray examination revealed definite skeletal changes in all of the cases. A few were considered negative at first, but the finding of typical myeloma cells in the sternal marrow led to a more careful search or repeated examination, revealing the presence of rarefactions. It is interesting to note that changes—usually rarefaction and occasionally tumefaction—involved more than one bone. These frequently led to a suspicion of metastatic malignancy and a vain search for the primary site.

J. H. Wright (37) was probably the first to report radiographic changes in this disease. His patient was a man, fifty-four years old, who entered the Massachusetts General Hospital because of a small tumor—of one year's duration—at the level of the nipple; other tumors developed later. Roentgenologic examination revealed changes in many of the patient's ribs. Bence-Jones' protein was present in the urine. Death occurred five months after admission, the diagnosis being confirmed by autopsy.

Bone Marrow Findings (Table II). All of our thirteen cases of myelomatosis were diagnosed by means of the sternal puncture. In some in-

stances the underlying condition had been suspected; in others the bone marrow findings were surprising and helped greatly in clearing up the diagnosis in obscure anemias, apparent leucopenic leukemias, so-called skeletal metastases, spondylitis and nephritis. The finding of myeloma cells often prompted further clinical and laboratory study of the case.

Prior to the employment of sternal puncture the diagnosis, on rare occasions, was made by means of a biopsy, as in the cases of Bloodgood, Perlzweig, Delrue and Geschickter, Gros, Zadek and Lichtenstein (38) and others. Within the past few years a ease in which the diagnosis was made by bone puncture has been reported by Bross (7), and sternal puncture by Markoff (24), Ferrata and Storti (10), Fleischhacker and Klima (11), (6 cases), and Varadi (7 cases), Schulten (30), (2 cases), Vogel, Erf and Rosenthal (34), (4 cases).

The marrow in multiple myeloma shows remarkable variations; the outstanding feature, however, is the presence of an increase in the number of large plasma-like cells. Normally such cells rarely exceed 0.5 per cent, but in myeloma they may increase up to 50 per cent (Ferrata and Storti) or 70 per cent (Fleischhacker and Klima). The marrow is usually cellular, and in only one case (Case 2) was it hypoplastic; a similar hypoplasia was encountered by Fleischhacker and Klima. The percentage of plasma cells varied from 3 per cent to 65 per cent in the present series. (Table II.)

The morphology of the cells in the marrow obtained by sternal puncture may be studied immediately and properly in stained smears. The predominating type is that of the plasma-like cells in twelve cases (Figures 1 and 3), and in one case the myelocytic type (Figure 4). The erythroblastic and the lymphocytic types of myeloma were not observed in our series, and none were reported by others who studied the cells in smears of sternal punctures. It is possible that both of these types may formerly have been misinterpreted in sections in which the morphology was misleading. These plasma myeloma cells differ from the plasma cells in the blood especially as seen in serum disease, infectious mononucleosis and in inflammatory areas. They are much larger in size; cytoplasm is considerably greater and does not assume the deep basophilic staining quality with the Giemsa stain and does not show the characteristic stain with Pappenheim's methyl-green pyronin. The myeloma cells show the characteristics of myeloid cells, whereas the genuine plasma cells resemble the lymphocytes.

In both the plasma and myelocytic types, the cells show a general eccentricity of the nucleus. In the plasma cells there is a variation in size from 7 to 14 miera in diameter (Figures 1 and 3) and they may contain a nucleolus; the nucleus of the myelocyte (Figure 4) may exceed these proportions. The cytoplasm of the plasma cell is deeply basophilic and may present variations in staining reaction, size and shape. It may appear irregular, with pseudopodia, round or faceted. It may contain a few azure

granules or appear vacuolated. A light perinuclear zone may be present in some cells (Figure 1). The oxidase reaction is negative in the plasma cells but present in the granular cells of myelocytic myeloma. Mitosis is occasionally seen. Some plasma cells may be extraordinarily large and may contain two to three nuclei (Figure 4). In supravital preparations, the plasma cells show an eccentric nucleus and a clear, homogeneous cytoplasm. Large dense mitochondria appear around the nucleus.

The Nature of Multiple Myeloma. Multiple myeloma may be regarded as a generalized systemic disease. The marrow of all bones is apparently involved, simulating to some extent the leukemic process. Practically all cases of multiple myeloma are aleukemic, that is, the peripheral blood does not reflect the changes in the bone marrow. Under exceptional circumstances the abnormal cells of myeloma may appear in the blood in the form of plasma-cell leukemia, as first reported by Gluzinski and Reichenstein (14) in 1906, and more recently by Osgood and Hunter (25), Patek and Castle (26). The blood picture, in myeloblastic and myelocytic myeloma, occuring in the present series, resembled a myeloid leukemia.

It is apparent that multiple myeloma is an interesting clinical entity, simulating a sarcomatous condition (Case 5) on the one hand and a leukemia (Cases 5, 10 and 13) on the other; it may assume the characteristics of both. On the whole it may present either an obscure or a well defined clinical picture with hematological and other laboratory findings which may either be misleading, or may lead to its identification. A definite diagnosis is possible during life only when made by means of sternal biopsy or the more simple aspiration method of Arinkin (1).

SUMMARY

1. Thirteen cases of multiple myeloma observed during the past two and one-half years are reported.

2. No characteristic findings were seen in the blood. A thrombocytopenia was present in five cases in the series; myelocytes and myeloblasts were present in some cases, especially the myelocytic myeloma.

3. The diagnosis in a number of cases was suggested by X-ray examination and the laboratory findings (hyperproteinemia, formol-gel reaction and Bence-Jones' proteinuria).

4. The underlying condition was revealed by simple sternal puncture.

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THE PHENOMENON OF TISSUE REACTIVITY IN THE KIDNEYS OF RABBITS*

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There are a number of important features which distinguish the phenomenon of local tissue reactivity to bacterial filtrates, as first described by Shwartzman (1), from the phenomenon of tissue reactivity in the kidneys of rabbits. In the former, the production of a state of preparedness for the phenomenon is obtained by the deposition of the bacterial filtrate locally, e.g., skin, stomach, knee joints, etc. The preparation of the kidneys for the phenomenon, however, may be obtained by one of three methods: (1) in a manner identical with that of the skin or other local phenomenon, namely, by direct injection of the bacterial filtrate into the renal parenchyma; (2) by introduction of the bacterial filtrate into the renal artery (Shwartzman and Baehr (2)); (3) by injection of the bacterial filtrate into the general circulation, usually through the ear veins (Gratia and Linz (3), Apitz (4), Gerber (5)). In all three instances, elicitation of the phenomenon is obtained by a second injection of bacterial filtrate into the general circulation. Recently, Moritz and Weir (6), in a study of the unilateral inhibition of the renal phenomenon following the direct introduction of the bacterial filtrate into the renal artery, produced a contralateral renal phenomenon. This method is comparable to the above mentioned third method, in that the filtrate, once having passed through the injected kidney, gains access to the general circulation; elicitation of the phenomenon in this instance is also secured by a second intravenous (ear vein) injection of the filtrate.

The first method above mentioned for obtaining the renal phenomenon requires no further discussion. The second method, in which preparation is achieved directly by way of the renal vascular system presents many similarities to the production of the phenomenon in the rabbit's ears by Shwartzman (7). The third method forms the subject of this report.

I. FACTORS INVOLVED IN THE PRODUCTION OF THE RENAL PHENOMENON

There are many similarities between the factors concerned in the production of the phenomenon of local tissue reactivity (skin, etc.) and

those involved in the production of the phenomenon in the kidneys. These will be described in brief and the features specific for the renal phenomenon will be pointed out.

A. *The Preparatory Factors.* The preparatory factors for the phenomenon are the same in all instances. Their nature and method of production have been described in detail by Shwartzman (8). The bacterial filtrates which were employed for purposes of preparation in the renal phenomenon were "agar-washings" filtrates of meningococcus, B. typhosus and B. coli. In the experiments to be described below, as well as in other published studies, these filtrates were titrated in terms of reacting potency for the skin phenomenon and expressed in units (Shwartzman (9)). The amount of filtrate used for intravenous preparation of the kidneys varied from 20 to 1000 units (.005 to 2.0 c.c. of "agar-washings" filtrate). Other investigators injected larger amounts, especially when working with broth culture filtrates. The preparatory injection was given by us in a single dose; others used divided doses, four to eight hours apart. The filtrate, in most instances, was diluted with physiological salt solution so that the desired number of units was delivered in one cubic centimeter of solution per kilogram body weight of the rabbit. Stock rabbits were used in all experiments.

B. *The Effects of the Preparatory Injection.* The effects of the injection of the preparatory factors upon the internal organs of the rabbit have been previously described by Gratia and Linz, Apitz, and Gerber. Renal lesions were not encountered with the preparatory injection alone except under special circumstances (pregnant rabbits (Apitz)). These will be discussed below.

C. *Dose of Filtrate.* The minimum dose necessary to secure preparation for the renal phenomenon, in our experiments, was 25 units; the minimum dose for the elicitation of the phenomenon was 100 units. However, somewhat larger doses were usually required. Because of the lethal effect, it was not possible to inject more than 200 units of meningococcus filtrate, or 1000 units of B. typhosus filtrate partially neutralized by homologous antitoxic horse serum (equivalent to about 500 units of non-neutralized filtrate). There appeared to be a greater incidence of renal lesions with larger doses of filtrate.

D. *Time Interval Between the Injection of the Preparatory and Reacting Factors.* An important element in the production of the phenomenon in any tissue or organ is the interval between preparation and elicitation. The optimum interval for the skin phenomenon is twenty-four hours, athough it may be reduced to twelve or prolonged to ninety-six hours. For the production of the renal phenomenon, the optimum interval between the first and second injections is usually twenty-four hours. Under similar experimental conditions, rabbits failed to show the renal phenomenon when the interval between preparation and elicitation was reduced to six hours, or increased to forty-eight hours.

It was thought that the addition of a substance which would increase vascular permeability might shorten the necessary interval between injections, inasmuch as Shwartzman (7) had shown that the phenomenon in rabbits' ears could be produced readily under such circumstances. A series of experiments was thus undertaken in which a potent testicular extract, known to be capable of enhancing vascular permeability, was injected intravenously together with the filtrates, or, in some instances, one hour prior to the injection of the preparatory factors. Despite some variation in time of administration and dosage the results may be summarized briefly as follows: Thirty stock rabbits were used and in three of these renal lesions were produced. In these three animals, the necessary interval between preparation and reaction was reduced from the usual twenty-four hours to between one and five hours. Aside from this time reduction, the administration of the testicular extract showed no other significant influences.

E. *The Reacting Factors.* The filtrates used as reacting factors in the experiments were identical with those used for preparation. It may be pointed out that, as in the phenomenon of local tissue reactivity, it is not essential to employ the same filtrate for reaction as for preparation; thus, B. typhosus filtrate may be used for preparation and meningococcus filtrate for elicitation. The use of the antigen-antibody complex as a reacting factor for the production of the phenomenon in the skin has been described in detail by Shwartzman (9). Negative results were obtained when tried in the kidney phenomenon (Gerber).

F. *The Use of Other Substances as Preparatory Factors.* Apitz had previously shown that pregnant animals required only a single intravenous injection of bacterial filtrate for the elicitation of the renal phenomenon, and assumed that pregnancy acted as a preparatory factor. We repeated the experiment, using 10 pregnant rabbits. Each received 100 units of meningococcus filtrate. One animal showed a focal renal lesion consisting of the presence of large, swollen glomeruli with capillary thrombi and early tubular necrosis. Although this single positive finding in ten animals is necessarily inconclusive, it is worthy of note inasmuch as this lesion had not been encountered previously with only a single injection of filtrate.

It was also decided to determine whether a preparatory effect in the kidneys could be obtained by the intravenous injection of living organisms, since it was previously shown in studies on the skin phenomenon that a state of preparedness existed in infected foci (Gratia and Linz (10), Koplik (11)). The following experiments were performed:

Material and Methods

Control Group (Group 1). A single intravenous injection of 3 or 4 c. c. of an eighteen hour old, 0.3 per cent glucose broth culture of streptococcus viridans (isolated from a case of subacute bacterial endocarditis) was given

to each of fifty-five rabbits. The animals were killed from one to six days later. Immediately prior to death blood was taken by cardiac puncture and cultured in plain and 2.0 per cent glucose broth, and in plain and 1.0 per cent glucose agar "pour" plates. The heart, liver, spleen, lungs, adrenals and bone marrow were examined grossly and microscopically in twenty-five animals, and the kidneys were examined in all. Sections were stained routinely with hematoxylin and eosin; bacterial staining was performed in some instances.

Control Group (Group II). Eleven animals received a single intravenous injection of 4 c. c. of a heat-killed eighteen hour old, 0.3 per cent glucose

TABLE I

Experimental Group—Summary of Protocols

NUM-BER OF ANI-MALS	TREATMENT RECEIVED	TIME KILLED	RESULTS OF BLOOD CULTURES				ANIMALS DIED	ANIMALS SHOW-ING RENAL LESIONS
			First		Second			
			+	−	+	−		
4	Streptococcus viridans, followed 24 hours later by 50 units meningococcus filtrate	24 hours later	4	−	1	−	3	0
11	Same organism, followed 48 hours later by 50 units meningococcus filtrate	24 hours later	7	4	4	1	6	2*
28	Same organism, followed 72 hours later by 50 units meningococcus filtrate	24 hours later	17	11	10	8	10	2*
8	Same organism, followed 72 hours later by 150 units meningococcus fil-trate	24 hours later	8	−	−	2	6	0
4	Same organism, followed 8 days later by 50 units meningococcus filtrate	24 hours later	1	3	1	3	0	0

* These animals died from 7 to 16 hours after the filtrate injection.

broth culture of the same organism and twenty-four to seventy-two hours later received, in addition, a single intravenous injection of fifty units of meningococcus filtrate. One day later the heart's blood was cultured as above and the animals killed. The organs were examined grossly and microscopically.

Control Group (Group III). Four animals were given a single intravenous injection of 4 c. c. of a Berkefeld filtrate of an eighteen hour old, 0.3 per cent glucose broth culture of the same organism and twenty-four hours later, in addition, a single intravenous injection of fifty units of meningococcus filtrate. One day later, these animals were killed and the organs examined.

Experimental Group. Fifty-five rabbits received a single intravenous injection of 3 or 4 c. c. of an eighteen hour old, 0.3 per cent glucose broth culture of the same organism. From one to eight days later the heart's blood was cultured, and immediately thereafter the animals received a single intravenous injection of 50 to 150 units of meningococcus filtrate. Twenty-four hours later the heart's blood of surviving animals was cultured again and the rabbits killed immediately thereafter. The internal organs were examined in forty-seven animals; the kidneys were examined in all. The protocols are summarized in Table I.
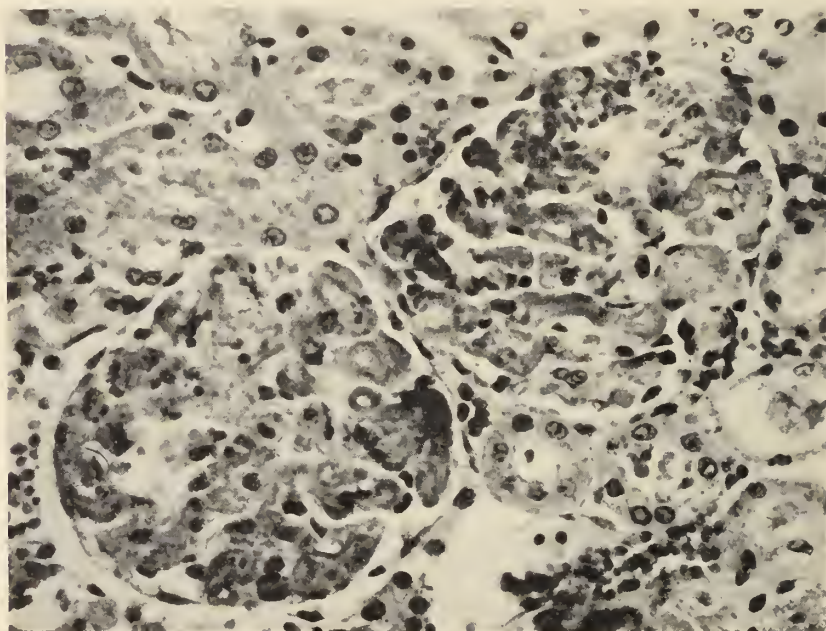
FIG. 1. Glomerular capillary thrombosis. The rabbit received 3 c.c. of an eighteen hour old, 0.3 per cent glucose broth culture of streptococcus viridans, followed forty-eight hours later by fifty units of meningococcus filtrate. The animal died sixteen hours after the filtrate injection.

Experimental Findings

The control group of animals showed the following changes. Seven of the fifty-five rabbits which received bacteria alone (Control Group I) presented focal collections of polymorphonuclear leucocytes in the renal medulla. Gram positive cocci were found in one instance. In the kidney of another animal in this group, a focal area of tubular necrosis was seen. There were no associated glomerular or vascular alterations. In one other instance, a focal glomerular lesion was found in one kidney. The appearance was that of a fusion of several capillary loops and about

the glomerulus there was a focal collection of round cells and polymorpho-nuclear leucocytes. The lesion resembled that described following injection of hemolytic streptococci. Only slight degenerative changes of the other internal organs were noted, such as are seen in untreated controls.

Rabbits which received heat-killed organisms, followed by a single injection of bacterial filtrate (Control Group II) presented scattered venous and capillary thrombi of the internal organs, exclusive of the kidneys. These changes are identical with those previously described when only a single dose of bacterial filtrate is given intravenously (Apitz, Gerber). Focal necrosis of the heart and liver were also seen, likewise similar to that previously noted following the injection of filtrate alone. Occasionally, such lesions were seen in untreated controls.

The experimental animals, which received both living bacteria and bacterial filtrate, also showed scattered venous thrombi in the liver, spleen, kidneys, bone marrow and lungs. However, in addition, four of these presented focal or diffuse capillary glomerular thrombi. The involved glomeruli were enlarged and the capillaries distended with thrombi and erythrocytes (Fig. 1). Some of the afferent arterioles also contained thrombi. There were marked congestion and focal hemorrhage in the interstitial tissue. The larger renal vessels were uninvolved. Bacteria were not found in the thrombi. As may be seen from Table I, two of the rabbits showing renal alterations had a positive blood culture and two a negative one at the time of filtrate injection. All showing renal changes died at periods varying from seven to sixteen hours after the injection of the filtrate. The renal alterations were recognized grossly in only one instance.

Discussion

In contrast to the changes just described, neither animals which died or were killed following single injections of bacterial filtrate nor untreated controls showed any renal alterations. Spontaneous renal lesions of this type have not been observed either by us or other investigators (Horn (12)).

Although the group with positive kidney changes, four in all, is too small from which to draw conclusions, it is interesting to note that it was observed in those animals in which filtrate was injected two or three days after the bacterial injection. The presence of a negative blood culture in two of the four animals, at the time of filtrate administration, does not preclude the possibility that a state of preparation was induced in the kidneys by the bacteria, since it is known that a state of reactivity for the local tissue (skin) phenomenon induced by filtrates can last for seventy-two to ninety-six hours or more (Shwartzman), and considerably longer in sites of local infection (Bordet (13), Gratia and Linz (3), Koplik (11)).

The filtrate of the organism used is known to have preparatory potency,

although a mild one. At the same time, the presence of the organism in the blood stream is compatible with an apparent well-being of the rabbit and can be found in the blood as long as eight days after injection.

These experiments may serve as a basis for throwing further light upon the pathogenesis of renal lesions in humans, inasmuch as nonpathogenic organisms, perhaps acting as secondary invaders, may be capable of eliciting a state of preparation in the kidneys.

G. *The Effects of Repeated Injections of Bacterial Filtrate.* In this experiment, repeated injections of filtrate were given over varying periods of time and the nature and fate of the lesions thus produced were observed. Meningococcus filtrate was used in all instances and administered intravenously. One group of twenty-two rabbits received daily injections and a second group of twenty-two received the bacterial filtrate on alternate days. The dose of the preparatory injection varied from five to twenty-five units; the second or reacting dose from twenty to twenty-five units. The interval between injections was six hours. The animals received from one to twenty-three injections, an average of 5.7 for the first group and 7.4 for the second group. The total amount of filtrate given varied from 50 to 300 units for the first group and 25 to 300 units for the second group. The average length of survival of the animals in the first group was 5.7 days, and approximately twelve days in the second group. The rabbits died or were killed within twenty-four hours of the last injection. All of the internal organs were examined. Since we are here concerned only with the phenomenon in the kidneys, the pathologic changes found in the other organs will not be described. Five animals showed renal alterations comparable to those found when a single intravenous preparatory injection of filtrate was given, followed by a single reacting injection. Microscopically, one of these animals showed scattered areas of calcification in the tubules and a second presented similar changes in the glomerular loops. Aside from this finding, which may be taken as an indication of a reparative process, no findings characteristic or indicative of chronicity of the lesions were observed. The primary renal lesions elicited by the preparatory and reacting injections of the filtrate were not intensified by the further injection of repeated doses of filtrate. Further studies, over still longer periods of time, would be required before definite conclusions can be reached.

II. THE MORPHOLOGY OF THE RENAL PHENOMENON

There is a great deal of variation in the extent of the lesions, in some instances dependent upon the method by which it is produced. When the lesions follow local vascular preparation, as described by Shwartzman and Baehr, there are massive hemorrhage and necrosis involving the entire kidney. The renal changes following the production of the phenomenon by way of the general circulation may vary from focal glomerular capillary thrombi to extensive hemorrhage and necrosis in the cortex and

at times involve the entire cortex. Associated vascular necrosis is also seen. The lesions may escape gross recognition and be found only microscopically in small foci. Not infrequently, primary tubular degeneration and necrosis are present with but slight glomerular involvement. Apitz and Gerber have published detailed gross and microscopic descriptions. When living organisms are used as preparatory factors, as described above, the predominant alteration is that of glomerular capillary thrombosis with focal hemorrhage and occasional thrombi in the afferent arterioles.

III. THE MECHANISM INVOLVED IN THE ELICITATION OF THE RENAL PHENOMENON

It appears, from all that has been pointed out above, that the kidneys alone, of all the internal organs, represent the only ones in which a state of reactivity can be said to have been elicited when the factors employed were similar to or identical with those of the local tissue (skin, etc.) phenomenon. This state of reactivity of the kidneys, therefore, is immunologically comparable to that of the local tissue phenomenon. The fact that in the kidney phenomenon preparation can be achieved by the local renal or general circulation requires especial mention. It may be possible to explain this fact by the natural permeability of the renal capillaries which permit or effect renal preparation, just as artificially induced vascular permeability in the rabbit's ears effects local preparation for the phenomenon (Shwartzman). The insusceptibility of other internal organs to a state of reactivity when filtrate circulates in the blood stream may be accounted for by a lower degree of vascular permeability. A further evidence that renal vascular permeability may be an important factor is found in the experiments of Stolywho (14), who showed that the filtrates are excreted in the urine of rabbits.

That vascular permeability is of considerable importance in the elicitation of the state of reactivity is shown by the fact that with the use of substances which increase the vascular permeability (testicular extract) the time interval between the preparatory and reacting injections may be reduced materially in the kidneys. It seems, therefore, that, as Shwartzman (9) has suggested, the renal form of the phenomenon is likewise a phenomenon of local tissue reactivity, the difference being in the fact that the preparatory factors when introduced into the general circulation find conditions inherent in its own vascular system favorable for the local preparation of the kidneys.

IV. THE SIGNIFICANCE OF THE RENAL PHENOMENON WITH REGARD TO ANIMAL AND HUMAN RENAL LESIONS

Lesions of the kidneys, closely resembling the changes described in the present studies, have been produced by the intravenous use of concentrated bacterial filtrates which are apparently not capable of eliciting

the phenomenon of local tissue reactivity, namely, staphylococcus toxin (Rigdon, Joyner and Ricketts (15), von Glahn and Weld (16)): Also, Roehrer (17) described similar renal changes in spontaneous hog cholera and was able to produce the lesion by the injection of the specific virus. In horses used for the production of anti-meningococcus serum, renal glomerular capillary thrombi are observed (18). In humans, cortical renal necrosis has been described in association with various types of infections such as diphtheria, scarlet fever, grippe, malaria, tonsillitis, etc. This occurrence of the renal lesions attendant on infections in animals and man, and their resemblance to the experimentally produced alterations in the renal phenomenon suggest an underlying related mechanism. The morphologic similarity of the spontaneous and experimental lesions, taken together with certain of the factors concerned in the production of the renal phenomenon, may serve as a basis for a further understanding of the pathogenesis of kidney disease in humans.

SUMMARY

The methods by which the kidneys of rabbits can be prepared for the production of the phenomenon of tissue reactivity are reviewed and the factors involved are discussed. A series of experiments are reported in which the following additional facts are demonstrated: 1) The necessary interval between the intravenous injections of preparatory and reacting doses of filtrate, usually twenty-four hours, may be reduced to between one and five hours by the additional administration of a substance known to enhance vascular permeability (testicular extract). 2) It is possible to achieve preparation of the kidneys for the phenomenon by the intravenous injection of living organisms (Streptococcus viridans). 3) Studies with repeated injections of filtrate over varying periods of time failed to show intensification of the lesion in the renal phenomenon.

The morphology of the renal lesion is described. The mechanism underlying the renal phenomenon probably depends upon the natural vascular permeability of that organ. Thus, the elicitation of the renal phenomenon by way of the general circulation probably represents a phenomenon of local tissue reactivity in which the filtrate, when introduced into the general circulation, finds conditions inherent in the renal vascular system favorable for local preparation. The significance of the renal phenomenon with regard to animal and human renal lesions is discussed.

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MULTIPLE PRIMARY CANCERS SUCCESSFULLY TREATED BY RADIATION THERAPY

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Multiple malignant neoplasms have been reported in increasing numbers during the past decade. Nevertheless, the incidence is still not large when one considers the large number of existing cancers. Murray (1) found one per cent of multiple primary malignant neoplasms in 4,219 post mortem examinations; Schreiner and Wehr (2) report an incidence of 2.7 per cent; Warren and Gates (3) found forty cases or 3.7 per cent in 1,078 autopsies. Other investigators report an incidence varying from 0.5 per cent to 3.5 per cent. In explaining this low percentage of incidence some authors held that the first tumor inhibited the development of a second. However, a more likely explanation is the fact that the patient may succumb to the initial growth before a second malignant tumor appears.

The finding of multiple primary tumors in the same subject according to Ewing (4) is nothing more than an accidental occurrence. Hanlon (5), in an investigation of 3,000 autopsies at the Mayo Clinic, found eighteen cases of multiple primary malignant neoplasms. He concluded that the condition was rare and found that the distribution among the various organs corresponded closely with the percentage distribution of carcinoma as it occurs when it is a single lesion. This fact, he feels, points toward coincidental occurrence of multiple neoplasms rather than a response to a definite law of formation of tumors.

Billroth in 1869 described a case of multiple malignant neoplasms and he postulated that two cancers found in the same organism may be considered as independent growths only (1) when they vary in structure; (2) when each tumor can be traced to its respective matrix; and (3) when metastases can be traced to the respective mother tumor. These requirements according to Fried (6) and others are difficult to fulfill and therefore lead to inaccurate estimates. For instance, two tumors of the intestines arising in different parts may have the same histology. Again, in bulky neoplasms involving contiguous organs, a second primary cancer may be overlooked. The third postulate can only be filled when each respective tumor gives metastases of its own. Sometimes the first cancer may heal and present no metastases and a second primary malignant growth may appear. Furthermore, basal cell epithelioma may be multiple and yet rarely metastasize.

Warren and Gates (3) point out that, as our knowledge of cancer increases, we are better able to distinguish the primary tumors from metastases and we can therefore liberalize the above requirements. They say that this will reflect more accurately the true incidence of multiple primary neoplasms because the former criteria resulted in a false low incidence. In their study, they used the following criteria: first, each of the tumors must present a definite picture of malignancy; second, they must be distinct; third, the probability of one being a metastasis of the other must be excluded. These criteria correspond closely to those previously suggested by Goetze (7).

The following case is being reported, first, because we believe that it presents two primary cancers, viz.: vaginal and anal; two, because of the favorable response of the vaginal lesion to radiation without the formation of a vagino-rectal fistula and the healing of the anal cancer.

FIG. 1.—Sagittal section showing involvement of recto-vaginal septum and anterior rectal wall

CASE REPORT

History (Adm. 353552). The patient was a sixty-two year old white widow who was admitted to The Mount Sinai Hospital on June 19, 1933. For six months she had complained of pain in the right buttock and the right lower abdomen which radiated to the posterior aspect of the right thigh. There had been no vaginal bleeding since the menopause which occurred ten years previously. She had ten children. The last pregnancy was twenty-seven years before admission. The past history was negative except for typhoid fever in 1915.

Pelvic examination revealed a multiparous introitus with senile atrophy of the vaginal mucosa. About seven centimeters from the introitus, on the right posterolateral vaginal wall, there was an ulcerated area three

centimeters in diameter. The base of the lesion was very hard and pene-
trated the recto-vaginal septum. On recto-vaginal examination, the
anterior rectal wall was ulcerated and the right parametrium was infil-
trated and thickened. The induration extended to the right pelvic wall
(see Fig. 1). The cervix appeared normal, the fundus of the uterus could
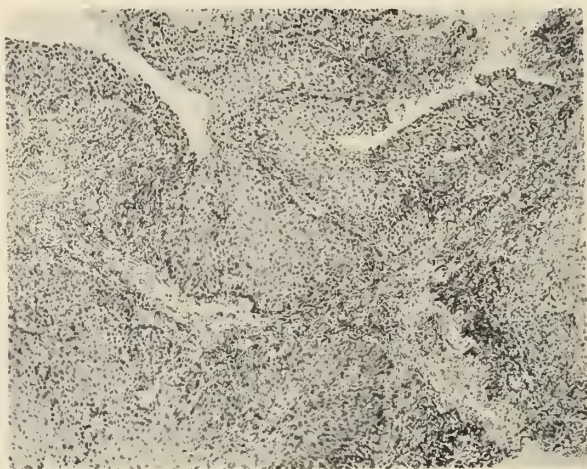
FIG. 2.—Vaginal biopsy showing medium ripe squamous cell carcinoma

FIG. 3.—Biopsy from rectum showing extension from vagina

not be defined. The left parametrium and para-vaginal tissues were
not infiltrated. The clinical diagnosis was carcinoma of the vagina,
stage IV. Proctoscopic examination revealed an eroded lesion of the
anterior rectal wall at the level of the vaginal mass (Fig. 1). X-ray exam-
ination of the spine and pelvis revealed no osseous metastases.

General physical examination was negative. The blood pressure was 136 systolic and 85 diastolic. Sedimentation rate was 60 minutes. Hemoglobin was 72 per cent. The blood Wassermann test was negative. The urine was negative.

Course. Biopsies from the vagina were diagnosed on microscopic examination, medium ripe squamous cell carcinoma (Fig. 2). A biopsy from the rectal surface showed the same type of carcinoma infiltrating the rectal mucosa (Fig. 3).

It was apparent that it was an instance of advanced carcinoma of the vagina which developed insidiously and remained symptom-free until the parametrial invasion caused the development of root pains. The prognosis as to cure and certainly as to avoidance of a recto-vaginal fistula was poor with any form of therapy. Naturally the primary aim was to destroy the lesion. We expected the production of a recto-vaginal fistula but planned our treatment to minimize this complication. The treatment was entirely by radiation therapy. All unnecessary trauma was to be avoided. To carry out this plan a course of external roentgen therapy around the pelvis was given first. This was followed by contact radium therapy to the lesion.

The patient received roentgen therapy to the pelvis from June 27, 1933 to July 3, 1933. The following factors were used:

K.V. 180*; M.A. 4; Filter 0.4 mm. zinc; 0.25 mm. copper; 1 mm. aluminum; Distance 60 cm.

Size of Portal

Anterior pelvis, 1200 "r"**. . . . . 20 × 24
Right gluteal, 1200 "r". . . . . 15 × 18
Left gluteal, 1200 "r". . . . . 15 × 18

On July 7, 1933 two capsules each containing 15 milligrams of radium element with a filter of 2 millimeters platinum and a secondary nonmetallic filter of a metal rubber 0.5 cm. thick were inserted into the vault of the vagina against the lesion. These were left in place for four days. A total dose of 2880 milligram hours was given.

The immediate reaction to the radiotherapy was an increase in the size of the recto-vaginal mass. The swelling gradually subsided and the ulceration healed. Nine months after treatment there was a complete disappearance of all gross evidences of disease and there was no recto-vaginal fistula. The patient remained asymptomatic until January 23, 1936 (two and a half years later) when she noticed a "lump" to the right of the anal sphincter. On examination, there was a hard, fissured exophytic growth, 3 cm. in diameter, involving two-thirds of the circumference of the anus. A linear thickening extended from the perianal mass into the

* Constant potential.
** Measured with back scattering.

right antero-lateral wall of the sphineter. The vaginal examination showed no signs of disease. Mieroseopie examination of the anal lesion (Fig. 4) showed a hornifying squamous eell earcinoma. Surgieal eonsultant advised perineal reseetion with the formation of an artificial anus but the patient refused this operation. Treatment by radiation therapy was therefore advised. Roentgen therapy was given in divided doses from January 27, 1936 to Mareh 23, 1936 as follows:

Factors used: Foeal skin distance 50 cm.; Filter 0.5 mm.; copper 1 mm.; aluminum.
   K.V. 180—constant potential.
   2000 "r"* to each of four gluteal fields 10 × 10 cm.
   1400 "r" to anal field direct, 7 cm. diameter.
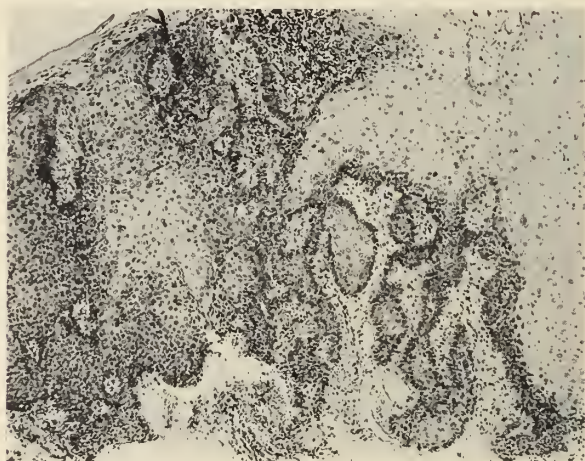
FIG. 4.—Anal biopsy showing hornifying squamous cell carcinoma

Within three months there was a complete disappearanee of the anal tumor and when last seen twenty-one months after treatment, (Oetober 1937) no gross evidenee of disease eould be deteeted.

COMMENT

The oceurrenee of two primary malignant neoplasms in the same individual is rare. Facts pointing to the presenee of multiple primary eancers in this patient were: first, both tumors were malignant and differed mieroseopieally (vaginal lesion, medium ripe squamous eell earcinoma; anal lesion, papillary hornifying squamous earcinoma); seeond, eaeh tumor was distinet; third, the seeond tumor originated in another organ (skin of anus). The interval between the appearanee of the two tumors was two and a half years. That the seeond tumor was not a metastasis

* r—measured in air.

was further substantiated by the absence of spread to the usually involved regional lymph nodes.

The absence of bleeding as the leading symptom was highly unusual in view of the extent of the primary lesion in the vagina. This may be explained by the fact that the patient was a widow and there were no marital relations.

The favorable response to radiotherapy of the vaginal carcinoma which is regarded as radioresistant, and the healing without the formation of a vaginorectal fistula, though the disease extended to the rectal mucosa, is unusual. The avoidance of trauma in the application of the radium was probably responsible for this. The patient is now well and free of gross evidence of disease four years after the detection of the initial lesion.

SUMMARY

A patient is presented with a vaginal cancer which extended to the rectal mucosa and which healed without the formation of a fistula after radiation therapy. The patient remained well for over four years after roentgen and radium therapy. Two and one-half years after destruction of the vaginal cancer, a second primary cancer of the anus developed which was destroyed by roentgen therapy without recurrence now for over a year and one-half.

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THE TREATMENT OF UNDESCENDED TESTES WITH GONADOTROPIC HORMONES

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A great deal of experimental work laid the foundations for the clinical use of the gonadotropic hormones. The investigations of Evans 'and Simpson (5), Smith and Engle (11), and Zondek and Aschheim (14) demonstrated that a gonad-stimulating principle is present in the anterior lobe of the pituitary gland. The discovery of Zondek and Aschheim of the presence of this gonadotropic principle in the urine of pregnant women was utilized by them in developing their test for the diagnosis of pregnancy. Engle (4) in 1932 described the experimental production of descent of the testes in immature monkeys by injections of hormones of the anterior pituitary gland obtained from pregnancy urine.

Beginning with Schapiro (9) in 1930, many accounts of the treatment of undescended testes in man with pregnancy urine extracts have appeared in the literature. Successful cases have been reported by Goldman and Stern (6), Sexton (10), Rubenstein (8), Cohn (2), Aberle and Jenkins (1), Webster (13), Dorff (3), and Spence and Scowen (12).

The following report is based on fifteen cases of cryptorchidism treated by the injections of gonadotropic hormones in the Out-Patient department of The Mount Sinai Hospital from July 1935 to July 1936. An additional follow-up period of one year was used to note any changes after the cessation of treatment.

A careful examination of the genitalia was made before starting treatment. In each case records were made of the size and position of the testes, the degree of development of the penis and scrotum, and the presence or absence of hernia. It is interesting to note that many cases referred for treatment were patients with mobile testes which could be brought into the scrotum by pressure over the inguinal canal. Such cases were excluded. The preparation of gonadotropic hormones used was "Follutein" (Squibb), a sterile glycerin solution of the anterior pituitary-like sex hormone found in pregnancy urine. The injections were given daily by the intramuscular route in each buttock. As suggested by Webster (13), the initial dose was 25 rat units. This was increased by 25 rat units each day until a dose of 250 rat units was reached. Thereafter the latter dose was continued.

Of the fifteen patients with undescended testes, the condition was

TABLE 1

CASE	AGE	GENERAL APPEARANCE	CONDITION OF TESTES BEFORE TREATMENT	TREATMENT		RESULT
				Total rat units	Time	
	years				*mos.*	
1	9	Normal	Right testis in lower third of inguinal canal-size 1.0 x 1.0 cm. Left testis in middle of inguinal canal-size difficult to determine because of large hernia	13,450	3	Right testis in lower scrotum-size 2.0 x 3.0 cm. Left testis unchanged
2	5	Underweight	Right testis in middle of inguinal canal-size 0.5 x 0.5 cm. Left testis in middle of inguinal canal-size 0.5 x 0.5 cm.	2,025	1	Right testis in lower scrotum-size 1.0 x 1.5 cm. Left testis in lower scrotum-size 1.0 x 1.5 cm.
3	6	Overweight	Right testis in middle of inguinal canal-size 0.5 x 0.5 cm. Left testis in lower third of inguinal canal-size 1.0 x 1.5 cm.	5,275	2	Right testes in lower scrotum-size 1.5 x 2.0 cm. Left testis in lower scrotum-size 1.5 x 2.0 cm.
4	14	Normal	Right testis in lower third of inguinal canal-size 1.5 x 2.5 cm. Left testicle in scrotum-size 2.5 x 3.5 cm.	13,200	3	Right testis unchanged Left testis unchanged
5	16	Normal	Right testis in middle of inguinal canal-size 2.0 x 2.5 cm. Left testis in middle of inguinal canal-size 3.0 x 3.5 cm. Mass of scar tissue in both inguinal regions due to previous operation	4,725	2	Right testis unchanged Left testis unchanged
6	11	Normal	Right testis in lower third of inguinal canal-size 1.0 x 1.0 cm. Left testis in scrotum size 2.0 x 3.0 cm.	8,850	3	Right testis same location-size 2.0 x 2.5 cm. Left testis unchanged
7	16	Hypogenital type	Right testis in scrotum-size 2.5 x 3.0 cm. Left testis in middle of inguinal canal-size 0.5 x 0.5 cm.	14,200	3	Right testis unchanged Left testis in lower third of inguinal canal-size 1.5 x 2.5 cm.

TABLE 1—*Concluded*

CASE	AGE	GENERAL APPEARANCE	CONDITION OF TESTES BEFORE TREATMENT	TREATMENT		RESULT
				Total rat units	Time	
	years				*mos.*	
8	11	Normal	Right testis not felt. Left testis in middle of inguinal canal-size 1.0 x 1.0 cm.	1,000	1	Right testis in lower scrotum-size 1.0 x 1.5 cm. Left testis in lower scrotum-size 1.0 x 1.5 cm.
9	13	Hypogenital type	Right testis in upper scrotum-size 1.0 x 1.5 cm. Left testis not felt	17,550	4	Right testis in lower scrotum-size 1.5 x 2.5 cm. Left testis in lower scrotum-size 1.5 x 2.0 cm.
10	4	Normal	Right testis in lower third of inguinal canal-size 0.5 x 0.5 cm. Left testis in scrotum-size 0.5 x 1.0 cm.	2,100	1	Right testis in lower scrotum-size 1.0 x 1.0 cm. Left testis unchanged
11	12	Hypogenital type	Right testis in upper scrotum-size 0.5 x 1.0 cm. Left testis not felt	5,200	2	Right testis in lower scrotum-size 2.0 x 2.5 cm. Left testis in lower scrotum-size 1.0 x 2.0 cm.
12	8	Normal	Right testis not felt. Left testis in scrotum-size 1.0 x 1.5 cm.	11,450	3	Right testis in lower third of inguinal canal-size 1.0 x 1.5 cm. Left testis unchanged
13	10	Normal	Right testis in lower third of inguinal canal-size 1.0 x 1.5 cm. Left testis in middle of inguinal canal-size 1.0 x 1.5 cm.	6,175	2	Right testis unchanged Left testis unchanged
14	7	Underweight	Right testis in lower third of inguinal canal-size 0.5 x 1.0 cm. Left testis in scrotum-size 1.0 x 1.5 cm.	6,375	2	Right testis in lower scrotum-size 1.0 x 1.5 cm. Left testis unchanged
15	12	Normal	Right testis in lower third of inguinal canal-size 0.5 x 1.0 cm. Left testis in scrotum-size 1.0 x 1.5 cm.	8,125	3	Right testis in lower scrotum-size 1.0 x 1.5 cm. Left testis unchanged
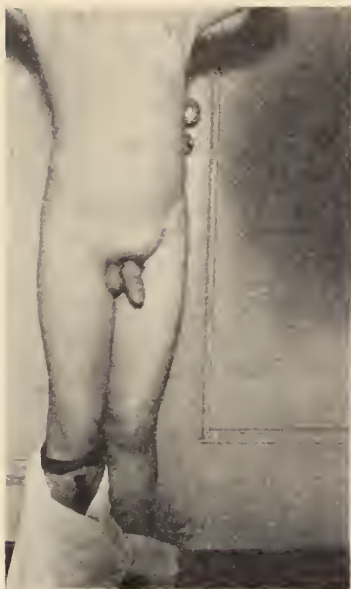
Case 1.   Case 2.
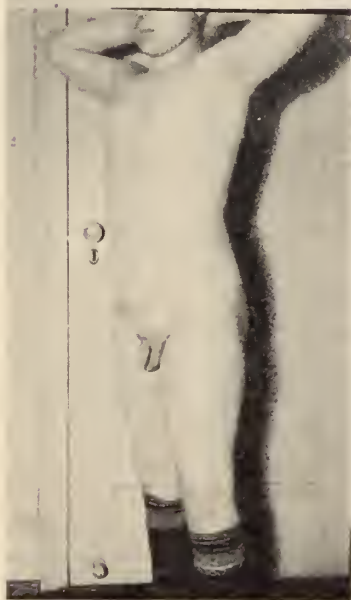
Case 9.   Case 11.

PHOTOGRAPHS ILLUSTRATING RESULTS IN CASES TREATED WITH
GONADOTROPIC HORMONE

bilateral in six.   In two it was unilateral with the other testis situated high in the scrotum, and in the remaining seven cases it was unilateral with the other testis situated low in the scrotum.   The age of the youngest patient was four years and the oldest sixteen years.

A summary of the cases is given in the accompanying table.   This shows that, of the six cases in which the condition was bilateral, in three instances both testes descended into the scrotum.   In a fourth case, one testis descended, and in the remaining two patients there was no descent of the testes.   In one of the failures, scar tissue in the inguinal canals due to previous operation prevented descent.   In the two cases in which the condition was unilateral and where the other testis was high in the scrotum, both testes descended well into the scrotum.   In the seven cases in which the condition was unilateral and where the other testis was situated low in the scrotum, the testis descended into the scrotum in three patients.   One case was partially successful, in that the testis which was not felt before treatment was brought into the lower third of the inguinal canal.   In three patients the treatment was unsuccessful.

In addition to descent of the testes, the injections of gonadotropic hormones produced other effects.   In most cases there was an increase in the size of the testes.   This was probably a factor in the causation of its descent.   A striking effect was an increase in size of the penis, most noticeable in the "hypogenital" type.   This was very marked in a few cases, as shown in the accompanying photographs.   After cessation of the treatment the penis became smaller, but usually remained larger than before treatment.   At the same time there was a noticeable development of the scrotum with increased rugosity, and in some cases a growth of pubic hair was noted.   Many children stated that there was some discomfort at the site of the undescended testes.   One child developed fever of 102 degrees F. and malaise.   Such reactions can be avoided by eliminating massive doses, and gradually working up the patient's tolerance by dosages such as were employed here.

There has been a report in the literature (7) of glycosuria following the administration of gonadotropic hormones in a child, aged 30 months. Dr. Lester Tuchman performed sugar tolerance tests in five children in this group and found no deviation from the normal.   In none of these children did he find a glycosuria.

SUMMARY

Fifteen patients with undescended testes were treated with large doses of anterior pituitary-like hormones extracted from pregnancy urine.   In six patients the maldescent was bilateral, in two unilateral with the other testis situated high in the scrotum, and in seven unilateral with the other testis situated low in the scrotum.   Of those cases in which the condition was bilateral both testes descended into the scrotum in three, one testis in one instance, while in two cases there was no descent.   Of the nine

cases in which the condition was unilateral, a descent of the testis into the scrotum occurred in five. One case was partially successful, in that the testis which was not felt before treatment was brought into the lower third of the inguinal canal. The testes have remained in the scrotum for one year after cessation of treatment. Other changes noted were enlargement of the testes and penis, development of the scrotum and growth of pubic hair.

CONCLUSION

The treatment of undescended testes with injections of gonadotropic hormones is advised. Failures are due to mechanical obstructions which should be treated by surgery, and in these cases hormone therapy is available as a valuable aid in the production of a successful result.

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ROUTINE TREATMENT BEFORE AND AFTER OPERATION ON THE COMMON BILE DUCT

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It has been known for many years that the high mortality following operation on the common bile duct was due in great part to the poor condition of the patient. The inability of the jaundiced patient to withstand the shock of the operation and the tendency to postoperative hemorrhage was notorious. It is only in recent years that a partial explanation has been given for these phenomena by the fundamental investigations into the physiology of the liver, and into the function of bile in digestion and absorption of foodstuffs.

The importance of these physiological investigations on the treatment of jaundiced patients was readily appreciated by surgeons, and the resultant findings were applied clinically. However, the gap between the theoretical conceptions and their translation into practical applications on the ward, has often resulted in haphazard procedures which occasionally would lead to the omission of important therapeutic measures.

ROUTINE PROCEDURE ON THE SURGICAL SERVICE OF DR. RALPH COLP

Following an extensive investigation into the pathologic physiology of the biliary tract, an attempt was made to establish a practical routine procedure which could be readily carried out on a patient in whom the common bile duct was drained. As a result of several years experience, the following procedures were finally adopted.

1. *Preoperative routine for one week.*
   (A) Twenty grains calcium lactate three times daily before meals.
   (B) One dram haliver oil and ten grains pure bile salts, between courses of each meal three times daily.
   (C) Fifteen grains compressed yeast tablets three times a day after meals.
   (D) High carbohydrate diet.
   (E) Transfusion, 500 c.c. citrate blood, one day before operation.
   (F) Continuous intravenous injection of 5 per cent glucose in normal saline. The infusion is started three days before operation, and continued throughout the operation and for the next forty-eight hours.

[1] Ralph Colp Fellow in Physiology.

2. *Operative routine.*

After exploration of the choledochus, a T-tube (size 20F) is implanted into the duct. The arms of the T-tube are shortened so that each arm is about 3 cm. long. This size T-tube is used even if the duct is very wide. If the duct is too narrow to admit a size 20 tube, a tube as large as possible is used. Before closing, the choledochus is pushed as far posteriorly as possible, and a rubber cuff slipped onto the tube to the level of the abdominal surface. Two safety pins are inserted into the cuff. Rubber dam drains are used for packing; gauze packs are used only if there is continuous oozing.

3. *Postoperative routine.*

(A) Continuous intravenous injection of 5 per cent glucose, alternating with normal saline solution, until the patient's oral intake of fluids exceeds the output.

(B) Transfusions: A blood transfusion is given if the patient's condition appears poor. In case of hemorrhage small transfusions of 200 c.c. are given daily. If biliary asthenia develops, with loss of appetite, nausea, dehydration, and a weak rapid pulse a transfusion of 500 c.c. of blood is given immediately.

(C) Twenty grains calcium lactate, fifteen grains yeast tablets, one dram of haliver oil, and sufficient bile salts to move the bowels at least once daily, are given three times a day. In general five grains of pure bile salts are given for each ounce of bile lost through the fistula.

(D) The rubber dam packing is removed on the fifth to the seventh day, to enable the fistula to close firmly around the T-tube as soon as possible.

(E) The bile from the T-tube is allowed to drain into an eight-ounce bottle attached by a short piece of tape to the abdominal binder.

(F) On the twelfth day after operation, when the T-tube is healed firmly into place, a lipidol X-ray examination is made of the biliary tract. This examination determines the presence or absence of spasm of the sphincter of Oddi, and the presence or absence of any organic obstruction. If no organic obstruction is present, the T-tube is tied off for two days. It is then opened and the resistance of the sphincter of Oddi measured manometrically. If the resistance is found to be below 100 mm. of water, the tube is removed. The fistula closes immediately without drainage of any bile, and the patient can be sent home the next day.

DISCUSSION

Administration of Calcium and Fat Soluble Vitamins. Considerable work has been done in the past to indicate that administration of large

amounts of calcium salts might be of some benefit in the prevention of postoperative hemorrhage in jaundiced patients. Although the evidence for that is not clear-cut there seem to be some indications that an increased calcium intake has some protective action on the liver cells and increases their resistance to toxins (1). Recent investigations have shown that calcium lactate taken by mouth is absorbed as efficiently as the more soluble types of compounds (2). Since 0.5–1 gram of calcium per day is the normal intake, the addition to the diet of about 0.5 grams of the calcium that is present in 4 grams of calcium lactate should be of some value. A greater intake than that might do some harm, since insoluble calcium soaps are formed in the intestinal tract and may prevent the absorption of fats.

Haliver oil is administered since it contains large amounts of vitamins A and D in a concentrated and fairly economical form. The work of Schmidt and his co-workers clearly demonstrated that absorption of these vitamins does not occur in the absence of bile salts from the intestinal tract (3, 4). Ivy showed that the administration of vitamin D tends to decrease the tendency to hemorrhage in jaundiced patients (5). Since bile salts are absent, or present in markedly diminished amounts, in the intestinal tract of patients with obstructive jaundice, there can be no doubt that there is very poor absorption of these vitamins in such conditions. Therefore, the administration of a large amount of the fat soluble vitamins A and D, together with a sufficient amount of pure bile salts, should lead to their absorption from the intestinal tract and be of some assistance both in overcoming the hemorrhagic tendency, and also in building up depleted body stores. In addition it has been shown that the administration of vitamin D also increases the ability of the intestinal tract to absorb calcium (6).

Carbohydrates and Vitamin B_1 as an Adjuvant. Whipple showed conclusively that a high carbohydrate diet exerts a markedly protective action on the liver cells (7). The administration of large amounts of sugar has therefore become a widely used procedure in the preoperative preparation of the jaundiced patient. The diet, however, is likely to consist almost exclusively of fruit juices and sugars and is hence almost completely deficient in vitamin B_1. The latter has been shown to be of great importance in the metabolism of glucose, and its deficiency leads to the accumulation of large amounts of lactic acid in the tissues (8). Also, the severely injured liver is often unable to transform efficiently lactic acid produced in the muscles into glycogen (9). Since there is no storage of vitamin B_1 in the body it would seem desirable, then, to supply the patient suffering from jaundice with an adequate daily intake of this vitamin. It is for this reason that forty-five grains of dried yeast are given to those patients daily.

Liver Function in Relation to Hemoglobin and Plasma Proteins. The

work of Whipple and his associates has shown also that the liver plays an important rôle in the manufacture of both hemoglobin and blood proteins (10, 11). Since the generation and destruction of blood proteins occur at a fairly rapid rate, injury to the liver for even a short period may cause depletion of blood proteins in the circulation. This results in blood concentration, so that patients suffering from severe liver disease are often found to have a hemoglobin of 100 per cent or more on admission to the hospital. Accordingly, a preoperative transfusion should never be omitted in cases of liver disease, since the determination of hemoglobin may be misleading and mask the necessity for such a procedure.

Technique of the Implantation of the T-tube. Our experience has demonstrated that a No. 20 F. T-tube is a satisfactory size for drainage of the choledochus. A larger tube tends to prevent firm healing of the fistulous tract around the tube, while a narrower tube occasionally becomes kinked or blocked with precipitated pigment. If the arms of the tube are too long, the lower one may protrude through the sphincter of Oddi into the duodenum, and occasionally allow a reflux of duodenal contents. In addition, if roentgen visualization of the biliary tract is attempted under such conditions, the lipiodol will pass directly into the duodenum without filling the ducts. We have one such case in which two common duct stones were missed because the common bile duct could not be filled with lipiodol.

In exposing the common duct there is a tendency to pull it anteriorly. The attached T-tube will hold the common duct in that position and so cause marked angulation. This can be prevented by pushing the choledochus as far posterior as possible before closing the abdomen, and fixing the tube at the level of the abdomen by two safety pins inserted into a rubber cuff. Adhesive tapes are attached to the safety pins on each side, giving ready access to that area whenever dressings have to be changed.

Treatment for Loss of Bile. Following operation, at least 3000 c.c. of fluid is given daily, in the form of 5 per cent glucose and glucose-saline. Calcium lactate, yeast tablets, haliver oil and bile salts are given in the quantities stated. If the loss of bile is more than about six ounces, an additional amount of bile salts is given. Since hepatic bile normally contains at least one per cent bile salts (12), in general about five grains of pure bile salts are given for each ounce loss of bile. This results as a rule in the patient having at least one spontaneous bowel movement daily. In the exceptional case the patient will tolerate the administration of the fistula bile by Levin tube. The total daily output from the fistula is divided into three portions and administered just before each meal. In such cases bile salts are not given.

The patient is usually given a transfusion immediately after operation. If hemorrhage, or marked oozing from the wound, occurs, small transfu-

sions of 200 c.c. of blood are given daily. Although the administration of
calcium and of vitamins is probably of some help, there can be no question
that our best therapeutic aid in the treatment of cholemic hemorrhage is
the repeated administration of small amounts of blood.

In the occasional case in which large amounts of bile are lost through
the fistula, the patient refuses both bile salts and bile. Such patients
often develop a severe form of asthenia, similar to pancreatic asthenia.
The first signs are the loss of appetite and a state of torpor. Nausea and
vomiting may then ensue. The pulse becomes rapid and thready and the
patient goes into a state of shock. Occasionally a markedly diminished
blood volume is found. A blood transfusion has a miraculous effect and
results in the immediate disappearance of all these symptoms. The cause
of this condition is unknown. It may be due partly to the loss of elec-
trolytes through the bile, or possibly to the diminution in the circulating
volume of blood as a result of diminished formation of blood proteins by
the damaged liver.

Visualization of the Biliary Tract. If the packings around the tube
are not kept in too long, the fistula will have healed solidly around the
tube by the twelfth day. The patient is then taken to the X-ray depart-
ment and, under fluoroscopic control, iodized oil is injected slowly into the
tube with a 50 c.c. syringe. The common bile duct and the terminations
of the hepatic ducts are seen to fill before the iodized oil passes through
the sphincter of Oddi into the duodenum. If the hepatic ducts fill to a
greater extent, our investigations have shown that the sphincter of Oddi
is spastic, i.e., that the resistance to the flow of bile into the duodenum
is more than 160 mm. of water (13). Two X-ray plates are taken, one
antero-posterior, and the other lateral.

The patient is then given gr. $\frac{1}{4}$ morphine hypodermically and five
minutes later iodized oil is again injected under fluoroscopic control.
The spasm caused by the morphine raises the resistance to the passage
of the oil into the intestine, and forces it up into the fine radicles of the
liver, outlining the whole biliary tract. Two more plates are then taken.
This procedure yields information on the patency of the bile passages,
the presence or absence of stones, and also as to the degree of spasm
of the sphincter of Oddi.

One technical point should be emphasized. One object of the visualiza-
tion of the biliary tract is to produce a roentgenogram showing the state
of tonicity of the sphincter of Oddi. Since the secretory pressure of the
liver is a fairly constant force of about 300–350 mm. of water (14), the limit-
ing factor which allows the biliary tract to fill to a variable extent is the re-
sistance of the sphincter of Oddi. The force of injection and the amount
of material introduced plays no important rôle, since, as soon as the
resistance of the sphincter of Oddi is exceeded, the duodenum will receive
any amount of a viscid fluid that can be injected through a narrow tube.
Therefore, in order to obtain a true picture of the forces involved and clear

outline of the whole biliary tract, there should be a continuous steady introduction of iodized oil while the roentgenogram is being taken. The danger of causing injury to the liver by the forceful injection of oil in the presence of organic obstruction, is obviated by doing the procedure under fluoroscopic control.

One investigation that had produced interesting results may be mentioned here. In all cases of common duct drainage the bile is examined for the presence of pancreatic enzymes, as evidenced by the presence of amylase. In a few cases this enzyme has been found in considerable concentration. Such findings serve as evidence of a reflux of pancreatic juice up the common bile duct, and can occur only if the pancreatic duct opens into the choledochus above the sphincter of Oddi. In all such cases of pancreatic reflux we have been able to outline the pancreatic duct by producing spasm of the sphincter of Oddi with morphine (13).

Conditions for the Removal of the T-tube. If no organic obstruction is found by roentgen examination the tube is tied off for a two day period. The patient is carefully watched for symptoms of undue distension of the common bile duct and for back pressure on the liver, as evidenced by epigastric distress or pain. Under such circumstances the tube is opened for brief periods. The closure of the tube imposes the full continuous force of hepatic secretion on the sphincter of Oddi and gradually causes a reduction in its tonus. Experimental work (15), and our own experience on humans, has demonstrated that a spastic sphincter suffers a rapid diminution in tonus under such conditions.

After two days, the resistance of the sphincter is measured in a simple fashion by attaching a straight glass tube to the end of the rubber tube. A 20 c.c. syringe with a needle attached, is filled with saline, and the needle introduced into the rubber tube. When saline is injected the column of fluid rises in the glass tube. As soon as the injection is stopped, the column rapidly falls until the manometric pressure equals the resistance of the sphincter of Oddi. This procedure is repeated several times to get an average level. Since the depth of the T-tube below the surface of the abdomen is known, the resistance of the sphincter is easily measured directly. A biliary fistula will close immediately if its depth as measured in millimeters of water is greater than the resistance of the sphincter, i.e., if the resistance to flow into the duodenum is less than the resistance of the column of fluid from the common duct to the surface of the abdomen. As a rule, the common duct is about 90–110 mm. below the surface. Therefore if the resistance of the sphincter is reduced to 90 mm., removal of the T-tube will result in immediate closure of the fistula.

If the resistance of the sphincter of Oddi is still too high after two days closure, the tube is tied off again for another two day period. There has never been any difficulty in the removal of a T-tube, even after a long continued implantation. We have had no success with the treatment of chronic cholangiolitis by long continued drainage of several months.

Attempts to Dissolve Residual Choledochal Stones. On a number of occasions we have tried to dissolve residual common duct stones by the injection of ether into the biliary tract (16). Neither these attempts, nor ones in which amyl nitrite was administered simultaneously (17) have in any way been successful. Even theoretically, such a procedure would be unsuccessful in about half the cases since the typical duct stone, found in 50 per cent of all choledochal stones, is composed almost wholly of calcium bilirubinate, a substance insoluble in ether.

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A CASE OF PROSTATITIS AND MULTIPLE ARTHRITIS OF DENTAL ORIGIN

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CASE REPORT

History (E. M. Adm. 289920). The patient, a male, aged 30, entered the hospital on April 14, 1928. Five months previously he developed a slight lumbago. Three months later he had an attack of severe pain in the sacral region and in the left hip, which radiated down the left leg. He was treated at another institution with baking and diathermy. X-ray examination of the spine at that institution showed a spondylitis, but was otherwise negative. X-ray pictures of the urinary tract were negative. Despite treatment the pain increased in intensity so that three weeks before admission to The Mount Sinai Hospital he took to bed, the pains being most severe in the left hip region, in the back and over the lumbar vertebrae. Two weeks later he developed urethritis. Smears of the urethral discharge were negative for gonococci. Pus cells were found in the urine. At about the same time a furuncle appeared over the left buttock. It was opened and was still discharging when he entered the hospital. He had been running a temperature between 99°F. and 100°F.

Physical Examination. His general condition appeared to be good. There was tenderness over some of the dorsal vertebrae and over the left hip region posteriorly. There was a small discharging furuncle on the left buttock which, on probing, proved to be quite superficial. The urine was clear with shreds in the first portion. The prostate was moderately enlarged and showed a small amount of pus on massage. The urethral smears were negative for gonococci; there were a few pus cells.

Dental Examination. A focal infection was suspected and a dental examination was requested. The findings were reported under the date of April 16, 1928 as follows: no deformities of the face; no periodonticlasia; teeth are in good condition with the exception of some large fillings in the upper right and in the left molars and lower right first molar. Radiographic studies revealed the following: lower right first molar root canals incompletely filled, with an area of infection at the root apices; upper right first molar root canals incompletely filled, with an area of infection at the root apices; upper left first molar root canals incompletely filled, with an area of infection at the root apices. In interpreting these findings the following facts are of significance. The root canal therapy was performed

over five years previously. The teeth had been pulpless many years previous to this treatment. The infected teeth were extracted and cultures from the root apices revealed a streptococcus anhemolyticus from which a vaccine was prepared and administered to the patient. ·

Course. Colonic irrigations, prostatic massage, bladder irrigations and diathermy were given with the patient's condition improving somewhat. He was still, however, running a slight temperature and there was still evidence of multiple joint involvement. The urine was examined bacteriologically on April 17 and reported to contain staphylococcus aureus, staphylococcus albus, streptococcus anhemolyticus and diphtheroids, but no gonococci were found. Complement fixation test for gonorrhea was negative. Blood examination revealed slight anisocytosis of the red blood cells. It was otherwise normal. Stereoroentgenograms of the spine from the seventh cervical vertebrae down to, and including, the tip of the coccyx, the pelvis, both hip joints and the ribs failed to show evidence of

LOWER RIGHT FIRST MOLAR; INCOMPLETE ROOT CANAL FILLINGS; AREA ON
ANTERIOR ROOT SUGGESTING INFECTION

myelomatous or other changes in the skeleton. Examination on April 20 of the prostate and vesicles showed fairly marked enlargement and, on massage, there was a moderate amount of pus expressed. Urine was cloudy. Urethral smears were negative. On the same day the lower right first molar was extracted. Culture revealed pure anhemolyticus streptococcus. There was no particular change in the systemic condition.

It was the conclusion of the physician in charge that there was possibly a focus of infection in the prostate gland and the teeth, both of which showed streptococcus anhemolyticus in pure culture. The patient was discharged from the hospital to be cared for at home.

I saw the patient in my office on June 4, 1928 and extracted the upper left first molar, from which cultures were reported to contain pure streptococcus anhemolyticus. On June 19 I extracted the upper right first molar which, on culture, yielded pure streptococcus anhemolyticus. Following the extraction of this tooth his temperature rose to 105°F. Blood culture taken at this time showed streptococcus anhemolyticus.

Dr. George Baehr, when he saw the patient, reported the following: "The patient suffered from severe arthritic pains in various joints of the

spine and extremities. He was discovered to have an infection of the prostate gland containing an anhemolytic streptococcus. The massage of the prostate revealed the presence of numerous pus cells, as well as the presence of these microorganisms. He was treated with prostatic massage and the fever and joint pains became worse."

The acute blood stream infection gradually subsided. After six weeks of rest the vaccine was given because he had slight pains in his joints. When seen on December 7, 1928 the prostatitis and arthralgia had completely disappeared. On December 18 the patient developed an acute appendicitis. He was operated upon by Dr. Neuhof who found a gangrenous appendix. A culture obtained disclosed streptococcus anhemolyticus and B. coli. He made a rapid and uneventful recovery.

COMMENT

The clinical diagnosis in this case was prostatitis and multiple arthritis. At first the teeth and gums were not considered a possible focus of infection, inasmuch as they presented no symptoms clinically. The roentgenograms, however, showed three teeth with incomplete root canal fillings, with slight areas of rarefaction at the root apices suggesting infection.

The fact that a root canal roentgenographically shows a complete filling does not mean that the canal is not infected; nor, when a canal is not completely filled does it mean that it is infected. The roentgenograms do not always show pathologic conditions. The only way a root canal can be tested as to its sterility is bacteriologically through the cultural method. Radiographs merely assist in the diagnosis and are by no means conclusive.

The dental-medical history is of utmost importance in making a diagnosis. In my experience there is an interval between the time a tooth becomes infected and the first expression of a systemic disturbance. The dental history invariably antedates the medical history. Patients may have infected teeth with old dental histories and yet may not have had a systemic disturbance for many years. It is no less important to treat the teeth in these cases.

The bacteriological findings in this case were very significant. The streptococcus anhemolyticus was recovered from the teeth, prostate, blood and appendix. The portal of entry for this organism is usually the oral cavity or upper respiratory tract. There is, therefore, no reason to doubt that the dental infection had existed asymptomatically for years and that it was the portal of entry for the infection of the prostate. The final convincing proof is that a transitory bacteremia followed extraction of one of the infected teeth. The multiple arthritis could have been the result either of the dental infection or the secondary prostatic infection with the anhemolytic streptococcus.

PERIOSTITIS AND OSTEITIS PUBIS COMPLICATING SUPRAPUBIC CYSTOTOMY

Report of Six Cases

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Only isolated references to periostitis and osteitis pubis have appeared in the literature. One finds no mention of it prior to 1924 when Edwin Beer (1) reported six cases before the Genito-Urinary Section of the New York Academy of Medicine. His precise description of this condition has since then served as a guide in its diagnosis. He (2) again reported this complication in a second paper in 1928 in which he stated that he had recognized one or more cases each year since 1916. The only other observations that we have been able to gather from the literature are those of Goldstein and Abeshouse (3), Kretschmer (4), Bucalossi (5), and Lazarus (6). Amongst the innumerable published papers concerned with complications that follow suprapubic cystotomy, only two (7) mention the condition under discussion.

Because of the scant attention that this complication has received, we are reporting six cases that we have been able to observe and which presented a typical picture of periostitis pubis, as described by Edwin Beer.

CASE REPORTS

We are reporting six cases which were seen in the Sinai Hospital, Baltimore, Maryland. They were all complicated suprapubic prostatectomies.

Case 1. H. J., age 68, presented typical symptoms of vesical neck obstruction. Cystoscopic examination revealed an intravesical prostatic enlargement. Two calculi were present in the bladder. His urine showed white blood cells, graded 2. A radiograph taken preoperatively demonstrated normal pelvic bones. A suprapubic cystostomy with removal of the two calculi was performed under spinal anesthesia. The space of Retzius was drained for forty-eight hours. Fascial necrosis of the wound developed, but rapidly disappeared. Three weeks after the first stage, the prostatectomy was done under spinal anesthesia. The suprapubic fistula had firmly healed eighteen days later and the patient was voiding freely. His urine at this time was clear.

Two months later, or fourteen weeks after the cystostomy, he returned, complaining of pain over the symphysis pubis and along the inner aspect of each thigh. Considerable tenderness was present over these areas. Adductor spasm was noted. His temperature was normal. Any attempt to sit down or stand up provoked excruciating pain. His gait was impaired. A roentgenogram taken at this time demonstrated a marked separation at the symphysis, with irregularity of the right pubic bone.

The patient was kept in bed and heat was applied locally. He improved very rapidly, so that ten days later he had no pain while at rest, although

Fig. 1 (Case 2). X-ray film shows complete fusion at symphysis. This is the condition after complete healing.

tenderness was still present. After the third month he was symptom-free.

Case 2. This patient was seen in consultation with Dr. Charles Levy. We wish to thank him for the privilege of reporting the case.

J. B., age 68, was admitted to the hospital with acute urinary retention. He had a typical prostatic enlargement. A suprapubic cystotomy was performed under local anesthesia. Two drains were placed in the space of Retzius. One was removed in twenty-four hours; the other after forty-eight hours. Nineteen days later a prostatectomy was performed. The patient voided nine days later and on the eleventh day the fistula had completely closed. The specimen was that of a typical prostatic adenoma.

Two weeks later, or approximately six weeks after the cystotomy, he began to complain of pain in the region of the symphysis pubis. Walking became difficult, and both thighs were adducted. An X-ray picture taken two months later showed a separation at the symphysis with marked atrophy and destruction of bone. The patient was placed in bed and diathermy was employed. He remained incapacitated for nine months, but finally recovered completely. A second roentgenogram was taken four months after the first and showed greater destruction of bone with new bone formation along the rami of the ischium. A third X-ray picture taken two years later showed complete fusion at the symphysis.

FIG. 2 (Case 3). X-ray film shows osteoporosis of the pubic bone

The following three cases were included in the publication by Goldstein and Abeshouse on "Prevesical, Perivesical, and Periprostatic Suppurations," but are here reported as typifying the complication under consideration in the present paper.

Case 3. H. T., age 64, was submitted to a one stage suprapubic prostatectomy, performed for prostatic enlargement. The space of Retzius was drained with iodoform gauze. Seven days after the operation a fascial necrosis developed. The urinary fistula persisted for fifty-one days. The patient was finally discharged in good condition with the wound firmly healed.

He was readmitted thirty-seven days later complaining of severe pain over the pubis. The slightest movement of the pelvis or the thighs was

extremely painful. There was marked tenderness along the symphysis pubis and the inferior rami of the pubis. A roentgenogram demonstrated small areas of osteoporosis of the pubic bone. Hot applications and massage were employed for two months, when the condition finally subsided, so that the patient no longer complained of any pain.

Case 4. H. W. R., age 58, was submitted to a two stage suprapubic prostatectomy, performed for prostatic enlargement. At the time of the first stage his urine showed infection. During this procedure, the space of Retzius was drained with iodoform gauze. The bladder was drained with a suprapubic tube placed high in the bladder incision. The second stage followed twenty-seven days later. At this time the space of Retzius was again drained for three days. The patient began to complain of pain along the inner aspect of the right thigh nine days after the second stage. This pain was attributed to a right vasitis. His urinary fistula closed on the twenty-sixth day. At this time tenderness was present over the symphysis pubis, and the patient complained of pain on moving his thighs. Adductor spasm was present. The wound was curetted down to the posterior surface of the pubic bone, and heat was applied. An abscess subsequently developed in the space of Retzius. This subsided rapidly after incision.

In this instance the osteitis was complicated by abscess formation. In view of our present experience in connection with this complication, it is likely that curettement would not be resorted to, as it was in this case.

Case 5. J. M., age 57. A diagnosis of benign hypertrophy of the prostate was made. At the first stage a drain was placed in the space of Retzius and a tube within the bladder. The prostate was removed nineteen days later and the space of Retzius was again drained. The patient began to void three weeks later. There was a purulent discharge through the suprapubic sinus for three months. The patient during this time developed adductor spasm, pain over the pubis and other characteristic symptoms of an osteitis pubis. In this case the pubic bone had to be thoroughly curetted before the suprapubic sinus would close.

Case 6. A. L., age 58, was admitted with a history of bladder neck obstruction of three years' duration, and a two stage suprapubic prostatectomy was done for a benign hypertrophy of the prostate. The space of Retzius was drained adequately in both stages. The suprapubic fistula was firmly closed on the twenty-second day and the patient voided satisfactorily.

One week later, or four and a half weeks postoperatively, he began to have pain over the pubis. There was some elevation of temperature. The suprapubic wound was opened and a small amount of pus evacuated. He subsequently developed bilateral adductor spasm of his thighs. An X-ray picture taken at this time showed an irregularity of the pubic bones. The posterior surface of the pubis required curettement. With

subsequent application of heat, the patient began to improve. He was incapacitated for three months, but finally was completely cured. A later roentgenogram showed the presence of new bone formation at the symphysis pubis.

From the paucity of reports that have appeared in the literature, one must conclude that this complication occurs rather infrequently. Although this is probably true, still we believe that many mild cases pass unnoticed; others, diagnosed, remain unreported. It would be advantageous to both urologist and orthopedist to become thoroughly familiar with this condition.

At the onset the periosteum covering the posterior surface of the pubic bone is involved. The condition then progresses to the body of the bone, where osteoporosis takes place. It may then proceed to the descending rami, and in some cases, to the ischial bones. In most instances repair occurs without progression to necrosis.

There has been no experimental work directed to the etiology of periostitis pubis following cystotomy. Various explanations have been offered. Incision into the bladder appears to be essential. The complication has never been reported after suprapubic exposures in which the bladder has not been opened. On the other hand, it has followed various procedures in which suprapubic cystotomy was performed—prostatectomy, bladder resection for carcinoma, and cystolithotomies. This fact suggests that infection arising from contamination with infected urine may be an important factor. Beer suggests that the periosteum may be injured either by traction on the attached recti muscles or by direct bruising of the periosteum, or perhaps, by the drainage tube inserted within the bladder. It has also been suggested that in some instances the periosteum may be injured by the needle employed in the local infiltration anesthesia. In some cases a very definite prevesical space infection antedates the bone involvement. Others, however, have presented no clinical evidence of such infection. It is our opinion that in all cases where the bladder is opened suprapubically, infected urine tends to seep down into the prevesical space. That space is, therefore, potentially infected, if not actually so. This source seems sufficient to initiate a periostitis of the pubic bone in such cases where the periosteum has been injured, perhaps in the fashion described by Beer.

Attention is not usually drawn to this complication until several weeks have elapsed after the cystotomy. In most cases the patient has already been discharged from the hospital and has been walking about without any difficulty. He suddenly, however, begins to complain of a pain over the body of the pubic bone. This pain becomes more pronounced and is particularly severe when the recti abdominis muscles are put on stretch. Thus, extension of the trunk on the pelvis causes extreme discomfort. As

the process extends along the descending rami of the pubic bones, the adductor muscles of the thighs become involved. Consequently walking becomes a great difficulty. The patient assumes an attitude of slight flexion and adduction of his thighs. Any motion of his pelvis or thighs precipitates agonizing pain. His gait becomes altered. At times, the process progresses to involve the ischial bones so that even sitting becomes extremely painful.

The physical signs are few. There is usually no rise in temperature, although there may be a slight elevation early in the course of this complication. Marked tenderness can be elicited over the body and the descending rami of the pubic bones, as well as along the adductor muscles which become spastic. Necrosis and suppuration rarely occur. Should this happen, however, as it did in Kretschmer's case, a sinus may form. There are usually no urinary symptoms present, although terminal dysuria has been reported as occurring in an advanced case.

In the early course of the disease there are no changes apparent on X-ray examination, but as the condition advances a roentgenogram will present rather significant changes. In such instance there will appear a fluffiness of the periosteum. Later, the osteitis is represented by an absorption of the bone. The pubic bones may appear separated at the symphysis.

Osteitis pubis must be differentiated from simple prevesical space infection without bone involvement. A distinction must also be made between it and a true osteomyelitis of the pubic bone. In the latter condition the temperature remains elevated and sequestration occurs. A most important differential diagnosis must be made from that of metastatic involvement of the pubis. When the periostitis first becomes apparent, clinically following prostatectomy, the surgeon is very apt to wonder whether the prostatic hypertrophy might not be accompanied by a carcinoma of that gland. Later, when absorption is observed in the roentgenogram, his suspicions are further aroused. In periostitis pubis, however, the osteoporosis is not accompanied by an osteosclerosis, which does occur in prostatic metastases of bone. Furthermore, the patient, after a period of disability, does become completely well.

Treatment consists essentially of complete rest and application of heat and massage. Both diathermy and hot sitz-baths are effective. It may be necessary to immobilize the pelvis and thighs in plaster. Fortunately, this condition usually responds to this regimen, and the symptoms gradually disappear within a period of two or three months. In some cases, however, they may persist for several years. Surgical intervention should be avoided unless actual bone necrosis occurs, in which case curettement is necessary. After healing occurs, the roentgenogram will reveal reparative changes of all involved areas. Osseous ankylosis may occur at the symphysis.

COMMENT

Six cases of periostitis and osteitis pubis have been presented. These complicated prostatectomies. The condition, although relatively rare, probably occurs much more frequently than one would infer from the paucity of reported cases. Both trauma and infection are probably instrumental in its causation. The clinical picture is so characteristic that a diagnosis should not be difficult. Pain over the involved bone and adductor spasm are outstanding symptoms. Positive roentgenographic findings demonstrating changes in the periosteum and bone itself will aid in establishing the diagnosis, but a negative X-ray film should not deter one from making such a diagnosis in the presence of a typical clinical story. The disease, fortunately, responds satisfactorily to treatment. Occasionally, however, the patient may be reduced to a life of invalidism for many months.

CONCLUSIONS

1. Periostitis and osteitis pubis is a complication that may follow any operation in which the urinary bladder is opened suprapubically.

2. The symptomatology is very characteristic and should readily lead to a diagnosis.

3. It is a self-limited condition which readily responds to local therapeutic measures.

4. Six illustrative cases are presented.

5. The profession is indebted to Dr. Edwin Beer for the original description of this disease.

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A CONSIDERATION OF THE PRESENT STATUS OF SUB-TOTAL GASTRECTOMY IN THE TREATMENT OF GASTRO-DUODENAL ULCERATION

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Although sub-total gastrectomy has been advocated for the past two decades as a procedure of choice in the surgical treatment of gastric and duodenal ulcer, no agreement exists concerning its actual and comparative merits. When the operation was first proposed, this radical approach was claimed to obviate gastro-jejunal and recurrent ulceration, complications particularly responsible for failure after more conservative measures. This beneficial effect was attributed to the removal of the ulcer-bearing area of the stomach and to the production of a gastric anacidity by eliminating the antral stimulating influence of the acid fundus glands. Disagreement with these contentions has been a minor factor in the present unsettled status of sub-total gastrectomy. The operation attracted particular controversial attention when its supporters, in arguing for its comparative advantages, imputed a prohibitive complicating incidence of gastro-jejunal ulceration to gastroenterostomy (17–34 per cent). After two decades of discussion the adherents of gastroenterostomy refuse to concede the frequency of that complication to be more than 3 to 5 per cent and contend that the greater inherent risks of sub-total gastrectomy nullify its asserted advantages. Attention has been so rivetted upon the issues of this controversy that in the evaluation of sub-total gastrectomy too little consideration has been given to the facts established by experience.

A discussion of the present status of sub-total gastrectomy from the latter point of view may be of interest. My impressions in this problem have been influenced to some extent by an association with the gastro-intestinal service at The Mount Sinai Hospital and by a particular interest in its follow-up results. Under the leadership of Dr. A. A. Berg in 1922, sub-total gastrectomy was adopted as a routine procedure for gastric and duodenal ulcers at that hospital, and as chief of that service he proved to be a foremost exponent of the operation. In view of that background, it is well to state that the purpose of this communication is not to support or refute any contentious point of view, but is rather to consider certain impressions which may contribute to a better understanding of sub-total gastrectomy.

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At this point it is pertinent to the purposes of this discussion to refer to the probable significance of the striking differences of opinion concerning the frequency of gastro-jejunal ulcer after gastroenterostomy. In the past it has received little or no attention. For a long time striking fallacies in the prevailing conclusions drawn from the statistical reports in this problem have been quite apparent, and I feel that a general indifference to them explains, to a great extent, the present confusion concerning the value of the operative measures employed for the treatment of peptic ulcer. Anyone who has read the recent series of articles on the "Principles of Medical Statistics" by A. Bradford Hill (1) cannot help but be impressed how strikingly the approach to this whole question illustrates the pitfalls inherent in statistical methods. It is not sufficient to publish results, as some observers do, and be content to ascribe their differences to a lack of uniformity in statistical methods. There must be sufficient objectivity to recognize the comparability of facts and the limitations of related conclusions. This is, admittedly, not easy in a disease, such as peptic ulcer, in which so many tangible and intangible factors may influence the ultimate end results of treatment. A study of the literature reveals such striking differences in the clinical material, the indications for operation, the type of operation, the pathological findings, the nature of follow-up observations, the evaluation of mortality figures and the methods of determining end results of treatment, to convince one of the practical impossibility of comparing statistical results. Under existing conditions it seems that the usual statistical results with any therapeutic measure are more apt to be reflective of an individual experience with a particular aspect, rather than with the ulcer disease as a whole.

The rationale advanced for sub-total gastrectomy attracted much interest because of its bearing upon gastric physiology and ulcer pathogenesis. Gastric acidity is recognized to be a most important factor in ulcer formation. It seems true that a peptic ulcer rarely, if ever, forms in the absence of free acid. Therefore, the creation of a gastric anacidity is a logical and desirable objective. But time and experience unfortunately have proved that sub-total gastrectomy does not uniformly produce a gastric anacidity, nor does it prevent recurrent ulceration. The studies of Eugene Klein (2) upon patients who had had a sub-total gastrectomy for duodenal ulcer revealed that 25 per cent of them showed anacidity, 41 per cent hypoacidity and 17 per cent hyperacidity. In contrast to the patients who were operated upon for duodenal ulcer, practically all gastric ulcer cases developed a true anacidity. The reason for this difference in postoperative anacidity after gastric and duodenal ulceration, while not apparent, may be of fundamental significance.

Four phases in gastric secretion are recognized: (1) the primary or psychic; (2) the secondary or gastric; (3) the intestinal; and (4) the continuous. The removal of the antral stimulus by sub-total gastrectomy

apparently only affects the gastric phase, and the acidity resulting from the other phases may be sufficient to permit recurrent or gastro-jejunal ulceration in individuals with an active ulcer diathesis. It is evident from postoperative studies that the beneficial effects of sub-total gastrectomy cannot be attributed to any specific influence on gastric acidity, but rather to a modus operandi, which may modify it by the removal of the antral influence and by the neutralizing effect of intestinal regurgitation and rapid stomach emptying.

As long as the etiology and the specific cure of peptic ulcer remain unknown, ultimate end results of treatment and the inherent risks are the indicators of the value of any therapeutic measure. It must be conceded that, unless 100 per cent of all cases are followed up for a sufficiently long period of time, the ultimate results of treatment cannot be known. Experience has shown that under present conditions it is almost impossible to accomplish this end, because a certain percentage of patients become lost to the clinic as a result of indifference or frequent migrations. At The Mount Sinai Hospital we have been able to follow only 50 per cent of our cases for periods of five years or longer. When it is appreciated that the evaluations of statistically and mathematically incomplete data vary most strikingly, it becomes evident that such results should not only be interpreted in terms of the method employed and that the deductions must be made guardedly. No matter how exacting the criteria for any particular method of follow-up study may be, if the data are insufficient, the results have a limited significance and cannot be reasonably compared with other statistics which are not based on comparable factors. Nevertheless this has been constantly done for the past two decades. This communication, therefore, has been limited to a consideration of the results reported from the Mount Sinai Clinic, and it reflects the ulcer problem as it is encountered at that clinic.

The follow-up results, previously reported by me,* related to a specific type of clinical material—ward patients, who for the most part were Jewish, who were engaged in arduous and confining occupations, and were exposed to unfavorable hygienic and economic conditions. The procedure routinely employed was a sub-total resection, which extended proximally from the level of the re-entrant angle of the lesser curvature of the stomach and distally included the ulcer-involved portion of the duodenum; gastro-intestinal continuity being re-established by a suture posterior gastro-jejunostomy according to the Hofmeister method. Follow-up observations were always made through personal interviews. In cases followed for at least five to ten years after sub-total gastrectomy for primary gastric and duodenal ulcers, 82.6 per cent remained free of symptoms; 13.9 per cent were improved but had mild symptoms, and 3.5 per cent were un-

* Fort-night—New York Academy of Medicine 1934.

improved. In the secondary cases representing recurrent and gastro-jejunal ulcerations after gastroenterostomy, 73.7 per cent remained symptom-free, 21 per cent were improved but had mild symptoms, and 5.3 per cent were failures. After sub-total gastrectomy for gastric ulcer the symptomatic results have been uniformly good, and it is significant that the procedure nearly always effected an absolute anacidity in this type of case. The results of sub-total gastrectomy were better in primary than in secondary cases, namely, those which had been subjected to a previous unsuccessful stomach operation. This would suggest that the ulcer diathesis, which had made a more conservative type of surgical procedure unsuccessful, is apt also to resist the beneficial effects of a sub-total gastrectomy. These results are especially significant because they lend themselves to a reasonable comparison with a series of cases of gastro-enterostomy reported from this clinic with a similar type of material. Lewisohn, in 1925 (3), confining himself to personal observations on cases of duodenal ulcer seen five years or longer after gastroenterostomy and examined within six months of making his report, found only 66 per cent of the patients to be improved by that operation, and 34 per cent to be suffering from gastrojejunal ulceration. In a similar type of follow-up study after sub-total gastrectomy, 92.3 per cent of the primary duodenal ulcers were found to be satisfactorily improved and 7.5 per cent to be failures.

It is not easy to evaluate the cause of symptoms following operations for peptic ulcer because many extraneous factors may contribute to vague gastric complaints. Thus, to minimize the personal equation in their interpretation, patients in our follow-up clinic are deliberately interviewed before a group of surgeons, gastroenterologists and members of the house staff. It was noted that persistent and severe recurrent symptoms after gastroenterostomy and sub-total gastrectomy are most frequently caused by recurrent and gastro-jejunal ulceration. Failures at our clinic have been specifically attributed to those factors. Of utmost interest is the frequency of gastro-jejunal ulceration after sub-total gastrectomy. Fifteen cases had been previously reported.* They established a minimal known incidence of 3.5 per cent for primary gastro-duodenal ulcers and 5.5 per cent for secondary ulcer cases. Inasmuch as there had been only a 49 per cent follow-up for cases of five years' or longer duration after operation, it was found impossible to draw any conclusion concerning the actual frequency of gastro-jejunal ulceration after sub-total gastrectomy. The comparative study based on Lewisohn's follow-up method revealed a 7.5 per cent incidence of gastro-jejunal ulceration after sub-total gastrectomy for primary duodenal ulcer in contrast to the 34 per cent found after gastroenterostomy. A. Bradford Hill has empha-sized in his work that, in dealing with statistical papers, it is probabilities

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* Fort-night—New York Academy of Medicine 1934.

that are weighed and it is not, as is sometimes suggested, a question of mathematical proof. If this is granted, the significance of the figures quoted seem to be in their proportional, rather than in their actual, value. The experience at The Mount Sinai Hospital gastro-intestinal clinic, seems to suggest that gastro-jejunal ulceration tends to occur four to five times more frequently after gastroenterostomy than after sub-total gastrectomy.

Inherent risk is a most important factor in the evaluation of any surgical procedure. The literature reveals mortality statistics for sub-total gastrectomy as strikingly divergent and as difficult to evaluate as those reported for the incidence of gastro-jejunal ulceration after gastroenterostomy. At The Mount Sinai Hospital Dr. A. A. Berg (4) in 1926 reported a 6.8 per cent operative mortality for primary duodenal ulcer and a 20.9 per cent mortality for secondary ulcer cases. He emphasized the importance of differentiating those two types of operative problems, stating that the results referred to a large series of patients (409) who were operated upon routinely with contra-indications reduced to a minimum. These results are reflective of the mortality of sub-total gastrectomy, when the procedure is routinely employed in the most experienced hands. In discussing the mortality after sub-total gastrectomy, Dr. Lewisohn (5) says, "The opponents of gastric resection have laid undue stress on the inherent high mortality of this operation. Undoubtedly some mortality statistics of 10 per cent or over have kept surgeons from adopting this method. Bohmansson's mortality of 3.1 per cent, Koenneeke's of 1.5 per cent, and my mortality of 2 per cent for partial and sub-total gastrectomy in primary gastro-duodenal ulcers compare favorably with the post gastroenterostomy mortality which is usually reported as between 2 per cent to 3 per cent." "Dr. Lewisohn's report related to a relatively small group of patients (60) for the most part without complicating factors. His results reflect the inherent risk of sub-total gastrectomy in uncomplicated cases." The mortality for the series of gastroenterostomies (primary and secondary) reported in 1925 was 4 per cent. It seems fair to state that sub-total gastrectomy, when routinely employed, is more hazardous than gastroenterostomy. Although the significance of this difference is still open to discussion, it seems to indicate that sub-total gastrectomy should be employed only after careful consideration of each individual case and not as a routine procedure.

Before choosing sub-total gastrectomy for any particular ulcer, consideration should be given to certain factors which experience has shown to increase its risks. Besides the well recognized factors of general condition, such as obesity, cardiovascular and respiratory disturbances, certain types of ulcers are recognized to contribute to an increased mortality. They are

represented for the most part by ulcers deep in the duodenum, posterior wall gastric and duodenal ulcers perforating into the pancreas, and high lesser curvature juxtacardial lesions. Cases which had been unsuccessfully treated by a previous gastric operation and those associated with massive uncontrolled bleeding are attended by a very high mortality rate.

It is fully agreed that certain types of ulcers are best served by a sub-total gastrectomy. This is particularly true of gastric ulceration, because of its very satisfactory postoperative results. Moreover, radical extirpation is advantageous in instances of questionable malignancy. Gastroenterostomy has not proved to be satisfactory in lesions proximal to the pylorus. It must be remembered that the mortality for gastric ulceration is higher than one usually appreciates. In juxtacardial lesions, it is prohibitive.

The greatest opposition to sub-total gastrectomy has been in the treatment of duodenal ulcer for the reasons already indicated. Inasmuch as gastroenterostomy satisfactorily improved at least 66 per cent of the patients at our clinic, it would be logical to restrict the more radical operation to the type of cases representing the 34 per cent of failures. Except possibly for the extremely emotional patients with high gastric acidities, it is not possible as yet to predict the fate of an uncomplicated active duodenal ulcer after gastroenterostomy. Unless the associated factors of risk contra-indicate, it seems logical to make sub-total gastrectomy the procedure of preference for the treatment of duodenal ulcer.

It is the prevalent opinion that peptic ulceration is most probably a constitutional disease. It is not unlikely that the success or failure of available therapeutic measures is determined by the degree of this inherent tendency which, at times, defeats every effort to overcome it. It is evident that sub-total gastrectomy has no specific influence on ulcer disease and must be regarded as a therapeutic measure which may favorably influence its activity. It is the experience at The Mount Sinai Hospital that this procedure has given more satisfactory results than other available measures and it is therefore justifiably regarded as the procedure of choice for the surgical treatment of peptic ulcer. However, its use should not be routine, but its selection should be the result of a careful consideration of the factors involved in each individual case.

In this communication attention has been drawn to certain facts which may permit a more reasonable understanding of the problems concerning sub-total gastrectomy. There has been no intention to evaluate the merits of the controversial issues that have arisen, but an attempt has been made to indicate some of the reasons for the failure to settle them in the course of the past two decades.

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URIC ACID RENAL STONES AND URIC ACID SHOWERS

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Uric acid stones and showers are not rare, but there is often great difficulty in their recognition, because of faulty interpretation of the clinical picture. Some years ago, in collaboration with Dr. Beer (1), I studied a series of one hundred and thirty-six renal stones, analyzed in the chemical laboratory, and found that about ten per cent of them were composed of uric acid and urates. Some contained urates and traces of calcium and magnesium salts. Except for a small percentage of the latter, which contain sufficient earthy salts to throw a shadow, uric acid and uratic stones are, on the whole, radio-transparent. Occasionally, if the uric acid stones are large and thick enough, they will throw a faint shadow on the film, but in obese individuals even this diagnostic aid is lost.

Attempts have been made by Dr. Beer (1) and others to coat a nonopaque stone with an opaque substance. This has been done by injecting argyrol, and Dr. Beer attempted to lay down an opaque coating on uric acid stones by means of artificial phosphaturia, but this was unsuccessful.

Therefore, a combination of methods must be used for diagnosis. Assuming that a patient with renal colic and an acid, non-infected urine, has an X-ray examination negative for stone, uric acid calculus or showers should be suspected. An attempt to demonstrate a "negative shadow," i.e., a filling defect in a pyelogram, is the first aid resorted to. Firstly, an intravenous urogram should be done, and this may or may not show a filling defect. Cystoscopy and retrograde pyelogram are next to be done. The output of indigo carmine is often delayed or diminished in concentration on the offending side, as is the case at times with renal calculi.

If a filling defect is found in the pyelogram, one must rule out other disorders presenting this picture. Blood clots can be removed by irrigation of the renal pelvis. Tumor of the cortex involving a calyx without renal distortion and papillary growths of the pelvis and calyces must also be excluded.

Passage of multiple wax tipped bougies is the method to use for exclusion of these conditions and confirmation of diagnosis of uric acid stone. If the wax tip is scratched, the diagnosis of stone is positive, and vice versa. Caution must be observed in interpreting a negative wax tip, for the position of a stone in a calyx or a narrow calyceal neck may result in no scratch. However, if a uric acid stone is suspected, passage of wax

tipped bougies should be repeated, in an effort to make a positive diagnosis. Negative results followed by positive scratch on later trial have been noted on occasion. It is only by such careful methods of diagnosis that the presence of uric acid renal stones may be determined and the clinical picture recognized.

Uric Acid Showers. This condition is also by no means a rare one, but it is often unrecognized. The clinical picture is that of renal or ureteral stone, with its attendant colic. The patient gives a history of lumbar pain, with typical radiation to the lower quadrant, either uni- or bilateral, or alternating on either side. The urine is generally clear, with no crystals present in the freshly voided specimen; microscopically it contains a few red cells, no crystalline elements, and is markedly acid, with a pH around 4.5.

X-ray examination and intravenous pyelogram are negative. Cystoscopy generally reveals a normal bladder, with no obstruction of either ureter. Retrograde pyelograms are negative, as are wax tipped bougies. The urine specimens from the kidneys are clear and free of crystals, while the indigo carmine excretion is normal. The blood uric acid is not elevated. But, on allowing the bladder and ureteral specimens to stand for twenty-four to seventy-two hours in sterile test tubes, there is a precipitation of dark brown crystals of uric acid on the sides of the tubes, containing the urine from the affected side or sides, and the bladder. On tapping the tube, the crystals rain down to the bottom and may be collected for microscopic and chemical examination.

Dr. E. Beer (1), in a paper on the subject, attempts to explain the failure to find crystals in the freshly collected urine, while they are found precipitated after leaving the specimen stand twenty-four to seventy-two hours. The uric acid is in a supersaturated solution in the urine, held in a solution of colloids. For reasons unknown, at the time of the colic these colloids fail to hold uric acid in solution, and precipitation of crystals results. The passage of these down the ureter gives us the clinical picture described above. These colloids are thought to be reversible, and crystals of uric acid redissolve in the urine, which, when collected, is therefore clear and crystal free. A diagnosis can only be made by allowing the urine to stand for twenty-four to seventy-two hours, after which time the crystals will be found.

Frequently, on questioning the patient as to his diet, one finds that he is primarily a meat and bread eater, one who avoids vegetables and fruits. In short, the patient has been on an acid ash diet and is found to have a typically intensely acid urine.

In all cases, even though uric acid crystals are found in the standing urine, a thorough urological examination must be made to rule out any condition which gives symptoms of ureteral obstruction with its attendant colic. Ureteral kinks, radiopaque stone without infection, so-called

and true strictures of the ureter, concomitant uric acid stone and extra-ureteral lesions, bearing pressure on, and obstructing the ureter, must be excluded. If such an examination is negative, and uric acid crystals precipitate on allowing the urine to stand, a diagnosis of uric acid showers is to be made.

The treatment is as follows. The patient's urine is alkalinized by putting him on the opposite of an acid ash diet Meat, fish and fowl, bread, cake, cereals, and cereal products are severely restricted The patient is instructed to eat plenty of vegetables, salads, and all fruits except plums and prunes. It is doubtful if the ingestion of exogenous uric acid plays any rôle in this condition.

If, after this diet is established, the urine is persistently acid, alkalis should be prescribed, and the reaction of the urine kept on the alkaline side, so that no more uric acid crystals can form. Another essential measure in the treatment is to maintain a dilute urine by having the patient take sufficient fluids, at least two quarts daily. Under such a regimen the symptoms are quickly relieved, and continuation of such therapy will obviate recurrence of uric acid showers.

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UROGRAPHIC STUDIES OF CALICEAL LESIONS

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The diagnosis of early localized or generalized kidney disease depends in many instances upon the radiographic study of one or more of the renal calices. It is important to recognize the initial manifestations of renal disease and to interpret correctly such manifestations if we are to treat lesions during the early stages. Thus, early nephrectomy in cases of malignancy before secondary involvement of the renal vein occurs is vital to the best interests of the patient.

As a prerequisite, it becomes necessary to familiarize oneself with the wide variety of appearances which the normal major and minor calices present. The major calices arise directly from the renal pelvis and may be two to five in number. Usually there are three; the superior, the middle and the inferior calices. The superior major calyx runs upward and somewhat laterally. The middle one runs horizontally outward and the lower one runs downward and somewhat outward. When the middle calyx is missing, the pelvis is usually bifid. The major calyx consists of (1) a base, which adjoins the pelvis, (2) a neck or isthmus and (3) the apex, from which the minor calices (one or two in number) arise. The minor calices are invaginated by the tips of the renal papillae to give the appearance of various degrees of "cupping." Occasionally the caliceal isthmus is unusually elongated so as to simulate the deformity produced by tumor. One or more of the major calices may be rudimentary, and the minor calices, though usually small, may be considerably enlarged. Contraction of the muscularis spiralis papillae (Muschat) which surrounds the base of the minor calyx and which is supposed to exert a milking action on the papillae, may prevent the filling of the minor calyx or produce the effect of isolation of the already filled minor calyx.

Whether the pyelogram be made by the intravenous or by the retrograde route, it is essential, for proper interpretation, that the pelvis and calices be adequately filled. The picture produced by incomplete filling may easily simulate that produced by renal deformity or a hydronephrosis may be overlooked. Overdistention of a pelvis by the opaque medium exaggerates the pyelographic appearance or causes reflex spasm and pain with consequent faulty pyelographic outline. Gentleness in cystoscopic manipulation and slow instillation of non-irritating opaque media into the kidney are essential. It is not uncommon to find a difference in the

appearance of the pyelogram produced by the intravenous (Fig. 1) and by the retrograde methods (Fig. 2). Proper evaluation of such pyelograms will be then rendered more difficult. Occasionally pyelographic study after a lapse of time may be advisable to obtain a better outline of the pelvis and calices to note whether any change has occurred since the previous examination.

Each of the various surgical diseases to which the kidney is subject usually produces a pyelographic outline peculiar to it. The earlier manifestations usually appear in the calyx. A description of the several X-ray patterns will be given elsewhere. However, no reliance must be placed

<div align="center">Fig. 1   Fig. 2</div>

FIG. 1. Intravenous pyelogram showing slight variation from the normal. Compare this with figure 2 in which the pyelogram was obtained on this side by retrograde instillation.

FIG. 2. Retrograde pyelogram in the same case as figure one, showing moth-eaten appearance of one of the middle calices (tuberculosis). This calyx did not appear in the intravenous pyelogram (fig. 1). The size of the individual calices varies in the two methods of pyelography in this case.

solely upon the urographic appearance. The history, physical examination and the various laboratory tests must corroborate the clue furnished by the roentgenogram. We shall not consider here the congenital anomalies, nor those cases in which changes in the calices occur, due to mechanical obstruction from the uretero-pelvic junction down to the bladder neck; nor those cases in which caliceal changes are produced by lesions outside of Gerota's fascial envelope.

Caliceal lesions to be discussed here are those which may be produced by:

1. Infections:
    a. tuberculosis,
    b. non-specific infections,
    c. cortical abscess of the kidney.
2. Mechanical factors:
    a. stones,
    b. strictures.
3. Tumors:
    a. intracaliceal and intrapelvic tumors,
    b. extracaliceal and extrapelvic tumors.
4. Miscellaneous causes:
    a. trauma
    b. conditions produced by disease in the circulatory system, such as infarction, etc.

The first three groups furnish the largest percentage of the cases, and hence shall be mainly considered here.

Tuberculosis (Figs. 3, 4, 5) reveals itself in the pyelogram in various stages, beginning with slight irregularity in the minor calyx, then presenting a more extensive moth-eaten appearance (renal necrosis), dilatation with or without a narrowing of the caliceal neck, occasional stricture and closure of such a neck with imprisonment of the tuberculous process and clearing up of clinical symptoms. The process may also produce more extensive changes with caseation and calcifications, and extension into the other calices or into the pelvis proper. Calcification and caseation may be noted on the plain X-ray plate in many instances. Any of the above X-ray findings must be checked by acid-fast stains of the urine sediment and, if necessary, by guinea-pig inoculations.

Non-specific infections due usually to the colon bacillus group of organisms may produce changes in the calyx closely simulating tuberculosis in the early stages. Here there may also be found slight irregularity, narrowing of the caliceal neck with hydro- or pyo-calyx. Repeated urine examinations by smear and guinea-pig inoculations, however, are negative for tuberculosis and one usually obtains on culture one of the colon bacillus group of organisms. The moth-eaten appearance of tuberculosis is not seen usually in these cases.

In many instances cortical abscess of the kidney may display definite spreading and encroachment upon two adjacent calices (Fig. 6). Cortical tumor may simulate the picture of cortical abscess, but the history, physical signs and laboratory tests should differentiate between the two conditions (Fig. 7).

The mechanical group is a frequent cause of intrinsic caliceal disease. Here are cases in which a stone has become impacted in a caliceal neck, producing various degrees of hydro- or pyo-calyx with loss of "cupping"

FIG. 3. Fairly early tuberculous process in one of the minor superior calices.   Note the irregularity and fainter dispersion of the opaque medium.

FIG. 4   FIG. 5

FIG. 4. Tuberculous involvement of the entire superior caliceal system.

FIG. 5. Separation of the inferior calyx from the pelvis with dilatation and "moth-eaten" appearance (tuberculosis).

(blunting) and consequent pressure atrophy of the renal cortex in communication with such a calyx. Occasionally such a stone may become impacted in one calyx, produce dilatation behind it, drop back into the pelvis, then become wedged in another calyx, and so on, producing several dilated calices. The pelvis in these cases is normal, unless the stone becomes wedged in the uretero-pelvic junction or in the ureter.

Extracaliceal renal tumors, such as hypernephromata and adenocarcinomata produce solid appearing negative shadows within the calyx if the

Fig. 6. A case of cortical renal abscess causing a "spread" of the superior and middle calices.

calyx is definitely invaded (Figs. 8, 9). The caliceal wall is "fractured," or the calyx may be obliterated completely. When there is no direct invasion of the calices, the earliest sign of solid renal tumor is an elongation with narrowing of the major and minor calyx, as the tumor draws the calyx out towards the periphery.

Intracaliceal uric acid stones produce negative shadows and may simulate the picture produced by tumor (Fig. 10).

Papillomata, papillary carcinomata, squamous cell carcinomata, may be found to have their beginning in a calyx. The papillary tumors produce

a "fluffy" negative shadow in the calyx (Fig. 11). This effect is caused by the dispersement of the opaque medium between the papillary fronds. As the tumors grow into the pelvis the extent of the negative shadow increases.

FIG. 7. "Spreading" of the upper calices, due to tumor at the upper pole (adenocarcinoma).

Polycystic kidney may simulate tumor in that there may be obliteration of calices or compression of calices by cysts and elongation. The usual palpatory findings of a bilateral tumor as well as similar bilateral pyelographic changes should help distinguish this condition from tumor. Solitary renal cysts, if large enough, may cause compression of the calices.

FIG. 8. Hypernephroma of the kidney with invasion of the superior calyx.   Note the "fracture" of the caliceal wall.

FIG. 9. Invasion of the lower calyx by adenocarcinoma of the cortex producing a negative shadow.

The form of the compression, however, usually assumes a more even, rounded outline.   Occasionally, it is true, differentiation from neoplasm may be difficult.

Fig. 10. "Negative" shadows in the lower calices due to uric acid calculi. Note the absence of the entire superior caliceal system. At operation, a complete cicatricial closure of the neck of the superior calyx was found with a large hydrocalyx of the upper pole whose cortex was reduced almost to a shell. Numerous small uric acid calculi were in the lower pole.

Fig. 11. Papilloma of the superior calyx extending somewhat into the pelvis Note the "fluffy" appearance of the shadow.

Trauma to either kidney may cause intrapelvic or intracaliceal hemorrhage with the formation of clots producing "negative" intracaliceal shadows. Vascular disease or blood dyscrasias may produce a similar picture, due to intrarenal bleeding.

SUMMARY

The urographic features of caliceal lesions are discussed with a view of evaluating the diagnostic leads they present. However, it is emphasized that complete studies of a case must be made in order to corroborate the disease pattern which the urographic appearance strongly suggests.

OPERATIVE X-RAY CONTROL IN THE SURGICAL TREATMENT OF RENAL CALCULI

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The surgical treatment of renal calculi fails in many instances to give satisfactory results, as judged by follow-up studies. The recurrence rates following conservative operation for renal calculus range from 4.6 to 60.0 per cent in the various clinics. These statistics depend on many factors, such as the types of cases considered, the duration and the accuracy of the follow-up observations, and the reliability of the reports.

A recent study of the operative results from this clinic (1) showed that for all types of cases—aseptic, infected, unilateral, bilateral, primary, and secondary—the true recurrence rates for pyelolithotomy, pyelonephrolithotomy, and nephrolithotomy were respectively, 14.9, 32.0, and 29.4 per cent; the residual recurrence rates were 10.6, 32.4, 41.4 per cent respectively, while the total of the true recurrence and residual recurrence rates were 24.0, 54.0, and 58.6 per cent respectively. These statistics were based on follow-up observations extending for an average of four years after operation. A differentiation was made between the true recurrences and the residual or pseudo-recurrences. The latter are classified as such when stones or stone fragments are known to have been present immediately after operation. The presence of residual calculi was determined by routine control X-ray examination taken at the time of the patient's discharge from the hospital after operation.

In order to reduce the incidence of recurrence after operation, the problem of "left-over" calculi or residual recurrence was attacked some years ago. Barney (2) was one of the first in this country to stress this point. In conservative surgery for multiple or dendritic calculi the use of a "kidney X-ray control" at the time of operation to help find stones or stone fragments which cannot be palpated or which have been overlooked has been emphasized by several authors.

Beer (3), in 1928, described his technic for the operative removal of stones under X-ray control. It is still used on his service. It took the place of fluoroscopic control (Brewer, Braasch) which had been used to determine the completeness of the removal of calculi. The latter was found to be unreliable since small stones were frequently recovered immediately after fluoroscopy had shown none to be visible. Following the lead of Quinby, films, which were immediately developed, were then

used and found to be much more practical. Subsequently, in collaboration with Dr. Benjamin of the X-ray department, Dr. Beer devised a small *cassette* and a boilable container for it, which could be placed behind the mobilized kidney. With three needles inserted in various portions of the kidney as guides or markers, an X-ray exposure is made and the film developed in a few minutes. The surgeon views the film, locates any stones or stone fragments by their relation to the markers and attempts their removal. During the operative procedure, several films may sometimes be needed. Besides being more accurate than the fluoroscopic method of control, one has a permanent record in the developed films. In some clinics, when the kidney cannot be mobilized, a large film is placed behind the kidney and the general region of the kidney exposed to the X-ray. The outline of the kidney is indicated by means of a bent probe which is placed around its periphery for this purpose. Although we, as yet, have had no experience with this method, it may serve as an additional aid in this work.

While it has been noted that the incidence of recurrence in this clinic is not low, it must be realized that, since the use of this technic, operative attempts to remove stones have been made in patients who previously would not have been surgically treated or would have been nephrectomized. This inclusion of more difficult cases in the group of patients treated by conservative operation would naturally increase the percentage of recurrence. Additional factors have been analyzed in the above-mentioned report (1).

In order to determine the value of operative X-ray control, patients who were subjected to operation in the years 1928 to 1933, were investigated. During the period mentioned, operative X-ray control was performed only on patients in whom the possibility of an incomplete removal of stones was hypothecated before operation. However, at the present time, operative X-ray control is used in all cases of multiple or dendritic calculi in which the kidney can be mobilized so that an X-ray exposure of the kidney can be made. Cases were encountered where even with only two stones visualized on the preoperative X-ray, additional small stone or stones were overlooked because they were hidden by the shadow of the larger stones. In addition, there were cases having what appeared on X-ray examination to be whole stones but which, in reality, were many small stones. Another reason for the more extended use of operative X-ray control is the fact that stones frequently change their position in the kidney. In spite of a roentgenogram taken on the day of the operation, the situation of the stone may have changed by the time the patient is operated upon. In such instances, an operative X-ray examination may be of great assistance in finding a small stone, especially one that cannot be palpated.

There were seventy-four patients with multiple or dendritic calculi upon whom a conservative operation was performed during the afore-mentioned period. Forty-one did not have an operative X-ray control performed. Of these forty-one, twenty patients (48.8 per cent) showed residual calculi. Thirty-three patients had operative X-ray control following which twelve (36.4 per cent) showed residual calculi (see Table). While the percentage of residual calculi is less in the cases which were controlled by operative X-ray, the difference is not as marked as one might expect. This, however, is due to the fact that there were ten cases in which stones or stone fragments were seen on X-ray control but could not be removed. In some of these ten cases, removal was not attempted because the patient's general condition did not warrant further prolonga-tion of the operation.

TABLE

To illustrate value of operative X-ray Control in Followed patients with Multiple and Dendritic Calculi

	NUMBER NOT PER-FORMED	RESIDUAL CALCULI		NUMBER PERFORMED	RESIDUAL CALCULI		HELPED LOCATE STONES OR FRAGMENTS NOT PALPATED	STONES OR STONE FRAGMENTS SEEN ON X-RAY CONTROL BUT COULD NOT BE RE-MOVED	NO FURTHER STONES SEEN ON DISCHARGE, X-RAY CONTROL		
		Number	Per cent		Number	Per cent			Number	Correct	Incorrect
Pyelolithotomy............	16	6	37.5	9	2	22	2	1*	7	5	2
Pyelonephrolithotomy....	14	5	35.7	18	7	38.9	10	6	12	11	1
Nephrolithotomy.........	11	9	81.8	6	3	50	3	3	3	3	0
Total..................	41	20	48.8	33	12	36.4	15	10	22	19	3

* Discharge X-ray control and subsequent X-rays were negative.

The real advantage of the procedure is demonstrated by the following consideration. In fifteen of the thirty-three cases with operative X-ray control, stones or stone fragments which could not be palpated or found without the roentgenograms were located and removed. In other words, if operative X-ray control had not been used on these fifteen patients, they would have undoubtedly shown residual calculi.

In twenty-two cases X-ray control showed no stones or fragments remaining in the kidney at the time of operation. This was proven to be correct in nineteen patients and incorrect in three, as verified by post-operative roentgenograms taken on the patient's discharge from the hospital. The percentage error in the case of a negative operative con-trol X-ray is then about 14 per cent.

CONCLUSION

Operative X-ray control is a valuable adjuvant in the operative treatment of multiple and dendritic renal calculi and should be used in all cases.

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RADIOPAQUE MEDIA IN UROLOGY

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Urography is the roentgenologic demonstration of the urinary system with the aid of media opaque to the X-rays. Historically, the clinical application of this field is intimately associated with the development and investigation of various opaque media. The substances under consideration may be classified as:

1. Colloids.
2. Crystalloids—which may be subdivided into the inorganic and organic iodides and bromides.
3. Gases—oxygen, carbon dioxide and air.

The pioneer attempts at delineating the urinary tract were made by Tuffier in 1897, by means of a mandrin passed through a ureteral catheter. Klose, in 1904, similarly used styletted catheters in a case of double ureter. In his report, he suggested the injection of an emulsion of bismuth into the pelvis and ureter through a catheter. The first one actually to have used an opaque medium was Keller, who, in 1904, demonstrated a bladder diverticulum made visible in the X-ray plate by means of the injection of air. In the same year, Wulff independently outlined the urinary bladder with the injection of a suspension of 10 per cent bismuth subnitrate. In 1905, Voelcker and von Lichtenberg used 2 per cent collargol for cystography, and in the following year they published their results on retrograde pyelography by means of this substance injected through a ureteral catheter, and were thus the first ones to outline satisfactorily the pelvis and calyces in the human with the X-ray. Subsequently other observers utilized stronger solutions of collargol. Argyrol, as well as a 5 per cent emulsion of silver iodide, were other silver compounds employed. Although in some hands the colloidal silver media have met with success, their use was finally abandoned, fatalities having been encountered. Braasch and Mann, injecting the pelvis of dogs, found that the silver preparations act as foreign bodies, frequently causing multiple foci of necrosis. Eisendrath, based on injecting known amounts of collargol under known pressure into the kidneys of dogs, believed that the majority of ill effects was due to the fact that when the capacity of the pelvis was exceeded by the injected fluid the solution was either forced into the loose tissues around the renal pelvis or into the renal parenchyma, and from there into the general circulation, with deposits in the various

viscera. At a pressure below 30 mm. of mercury he found that practically no collargol enters the kidney parenchyma or infiltrates the peripelvic tissues of the dog. However, at higher pressures, and when the capacity of the renal pelvis is exceeded, serious results may follow, such as, large infarcts, or small deposits of silver in the kidney or peri-renal tissues, infarcts, deposits or hemorrhages into the spleen or liver, and various lung changes—emboli, hemorrhagic infarcts, pneumonia or acute pulmonary edema. Collargol has been found to cause death from urinary suppression and hemorrhages from the bowel, mouth and nose in the human. It is obvious then, that the choice of a medium for retrograde pyelography becomes a very serious consideration since any over-distention of the renal pelvis may produce an invasion of the local and general circulation.

An improvement on the colloidal silver media came with the introduction by Burns in 1915, of the first crystalloid, a 10 to 15 per cent solution of thorium nitrate dissolved in sodium citrate and made neutral with sodium hydroxide. Associated irritative phenomena, occasional fatalities, its toxicity on standing, and the ease with which moulds grow in it, were some of the objections raised to it. Yet, for want of a better medium, it was the one of choice for three years.

A notable advance occurred in 1918 when Cameron suggested sodium and potassium iodide, and Weld proposed sodium and potassium bromide. The potassium salts in both cases were excluded because of the depressant effect of the potassium-ion, particularly on the heart. With regard to the comparative value of sodium iodide and sodium bromide for pyelography, Cameron, in a carefully detailed work proposed the former on the following grounds:

1. Its greater molecular weight, giving a radiographic shadow of greater density with a solution at much lower concentration.

2. Iodine is a member of a group of elements which possesses the property of selective absorption of the X-ray, particularly those of high penetration. Iodine shows an opacity to X-rays beyond what its atomic weight would indicate. Cameron found that one iodine atom has the opacity of three bromine atoms to the hard rays.

3. A 13.5 per cent iodide solution is as opaque as a 25.2 per cent sodium bromide solution, and more opaque than the standard thorium solution.

4. The osmotic pressure of sodium iodide in the concentration used for pyelographic purposes is only slightly greater than that of concentrated urine, and of all the various substances used, is the least hypertonic.

The question of hypertonicity becomes important when the work of Graves and Davidoff is taken into account. They observed, with the injection into the urinary bladder of rabbits of 40 c.c. of 25 per cent

sodium bromide at 17.4 mm. of mercury pressure that there was an in-
creased irritability of the vesical musculature which gave way to a distinct
depression. As the filling of the bladder progressed, its posterior wall
developed a pale, silvery sheen; the musculature became blanched as if
anemic. With greater distention there developed extreme edema which
involved the posterior dependent portion of the bladder and extended
into the adjacent tissues. Thrombosis of small vessels occurred at times.
When emptying was permitted they found the bladder completely crippled.
The anterior wall, however, protected by the air-bubble and away from
the solution contracted normally. These findings they could reproduce
using 36.4 per cent sodium iodide and 25 per cent sodium chloride solutions.
On the other hand, physiologic bromide solution, isotonic with blood, was
of no more effect than isotonic sodium chloride. They also reported that
14.5 per cent sodium iodide solution was innocuous from the standpoint
of the effect of hypertonicity and yet yielded good X-ray plates.

The arguments for the use of sodium iodide given by Cameron, are as
follows:

1. That in 25 per cent strength, like sodium bromide, sodium iodide
   produces no apparent immediate effect on the blood pressure and
   respiration when 50 c.c. are given intravenously to a thirty pound
   dog in a period of ten minutes.
2. That the kidney function as determined by the usual method is not
   affected by the injection of a 13.5 per cent sodium iodide solution into
   the kidney pelvis, even when experimentally the latter was kept
   distended at the secretory pressure of the kidney for twenty-five
   minutes. The same results were obtained with a 25.2 per cent
   sodium bromide solution.
3. The low viscosity of a 13.5 per cent sodium iodide solution approaches
   that of water. This makes for easy introduction and withdrawal.
4. Sodium iodide solution does not cause precipitates when mixed with
   urine.
5. It is neutral in reaction.
6. It yields satisfactory urograms with no serious reactions, 13.5 per
   cent sodium iodide being equal in opacity to 25.2 per cent of sodium
   bromide.
7. It is relatively inexpensive.

In passing, mention should be made of the other media and procedures
advocated in the past and which, in many instances, were subsequently
discarded:

A. *Media:*

1. The use of oxygen, air or carbon dioxide. Objection to the gases
   are their confusion with overlying intestinal gas, the difficulty of
   maintaining full distention of the pelvis and ureter, and air embolism.

2. Umbrenal or Lithium Iodide. This solution is expensive and frequently irritating, producing spasm of the calyces and pelvis, making interpretation of a pyelogram at times difficult.
3. Lipiodol is of an oily consistency, has a tendency to globule formation in the presence of aqueous solutions, is unsuitable for pyelography and is expensive.
4. Umbrathor, a colloidal suspension of thorium dioxide, is viscid, like lipiodol, making emptying by the renal pelvis difficult, and, in cases with mild upper urinary tract obstruction, becomes a source of irritation. Its use in cystography, however, has definite advantages. In one case in particular, that of a flat submucosal type of bladder carcinoma in which sodium iodide as a cystographic medium did not depict the filling-defect, the umbrathor, on the other hand, very concretely demarcated the circumference of the growth. The question of emptying of the medium in the case of the bladder is of relatively no consequence.
5. Neosilvol, in 20 per cent concentration has objections similar to lipiodol and umbrathor.

B. *Procedures:*

1. Perirenal and pericysto-pneumoradiography, the injection of oxygen, CO_2, or air around the kidney and bladder respectively, advocated by Carelli and Rosenstein independently, had been practically discarded because of the meagre information obtained and, above all, because of the general feeling of the attendant danger of air embolism and infection. Of late, however, perirenal pneumoradiography has been revived by Cahill and later by Mencher in the visualization of tumors of the adrenal gland, and of the renal outline.
2. Pneumoperitoneum, the injection of oxygen into the peritoneal cavity for the differentiation of intra- and retroperitoneal masses is unnecessary in most instances and, at times, coupled with danger.
3. Pyeloscopy, advocated by Legueu in Paris, and by Manges in this country, although satisfactory as practiced by them, is in most hands very unsatisfactory and unreliable, besides involving unnecessary exposure of the fluoroscopist.
4. The coating of non-opaque renal and ureteral stones with the injection of 2 per cent collargol and its subsequent aspiration has been shown to be unsatisfactory in the majority of cases.
5. Arteriography, introduced by Dos Santos, injecting iodide solution into the aorta under spinal anesthesia, thus outlining, in addition to the abdominal vessels, the renal arteries, is considered by most urologists not only superfluous but formidable and dangerous.
6. The visualization of the seminal vesicals by means of the injection of opaque media through the ejaculatory ducts has in most instances been difficult and not entirely helpful.

On the other hand, the following procedures which have withstood the test of time are worthy of consideration:

1. Cysto-urethrography is of aid in the visualization of bladder diverticula, urinary bladder stones, bladder tumors, extra-vesical intrusions, prostatic conditions, vesico-ureteral reflux and conditions affecting the urethra. The following technique is employed: The bladder, after being emptied with a catheter, is filled to the point of slight discomfort with a 3 to 5 per cent solution of sodium iodide or any of the organic iodide compounds. Exposures in the antero-posterior, and oblique or lateral positions are made. The bladder is then emptied and filled again with air, and another antero-posterior roentgenogram is obtained. In cases of suspected vesico-ureteral reflux, an additional film is made in the Trendelenburg position.

2. *Retrograde Pyelography.* A 12 per cent solution of sodium iodide or 40 per cent of any of the organic iodide substances is carefully injected through the ureteral catheter, preferably by gravity, at a pressure not above 20 mm. of mercury, until the patient complains of a fullness in the kidney region, or with the hand syringe under vision until the indigo carmine-stained medium is seen at the ureteral meatus, when simultaneously roentgenograms are made. In order to obtain a ureterogram, another exposure is made after injection, with the catheter withdrawn to the 5 cm. mark, and observing the efflux of the indigo carmine-stained medium. The latter enables one to visualize both the status of the ureter and its relation to the pelvis, as well as negative shadows caused by non-opaque stones, tumors, blood clots and the condition known as ureteritis cystica. Finally, in specified cases, an additional exposure is obtained after the catheter is withdrawn and the patient has been in a sitting position for fifteen minutes, in order to determine trapping of the renal pelvis as occurs in those cases where there is an aberrant vessel at the uretero-pelvic junction, and in ptosis of the kidney. In performing retrograde pyelography, an attempt should be made to avoid the so-called "pyelovenous backflow"—the forcing back of the pelvic contents into the veins overlying the fornices under conditions of moderate intra-pelvic pressure. The importance of pyelovenous backflow arises from the difficulty introduced into the interpretation of the roentgenograms, particularly their differentiation from the pyelographic appearance in renal tuberculosis and renal neoplasm. The question of so-called pyelovenous backflow, aside from being a very intriguing one, experimentally and clinically, probably also accounts for the systemic reactions observed following retrograde pyelography. According to Hinman and Lee-Brown, the degree of back pressure producing it is generally less than the secretory pressure which in dogs is about 63 mm. of mercury. They

state that it is not an extravasation, but has a definite route confined to the veins, the point of actual communication of the pelvis with the venous system being from the minor calyces at the base of one of the pyramids. Experimenting with the fresh kidneys of the dog and rabbit under manometric control, they observed that the lower limits of distention producing pyelovenous backflow is 20 mm. of mercury, depending of course on the duration of maintenance of that pressure. A pressure much beyond the maximal secretory pressure, however, commonly produces parenchymal extravasation. In vivo, they showed that phenosulphonphthalein injected into a dog's pelvis at a pressure of 40 mm. of mercury appeared shortly from the opposite kidney as well as in blood. Subsequent examinations of the kidney showed no break or area of extravasation. Bird and Moise, on the other hand, concluded from their experiments that a backflow of fluid from the renal pelvis into the tubules and Bowman's capsules may occur under conditions of moderately increased intra-pelvic pressure; that if a backflow of pelvic contents into the venous system of the living animal ever occurs, the probable mechanism is by rupture of tubules into the larger strait and arcuate veins intimately related to them.

Retrograde pyelography is considered contra-indicated in the presence of acute urinary infections and in cases of renal decompensation. In most institutions, bilateral pyelography with the inorganic iodides is not performed at one sitting. The dangers associated with this procedure may be shock, infection, general sepsis, anuria, chemical poisoning, local irritative phenomena and death. With the advent of organically bound iodide urographic media, their innocuousness when given in large doses intravenously and the relative absence of iodism, constitutional and local reactions, sodium iodide has been discarded in most institutions.

The Development of the Organic Iodides and Their Present Rôle in Urography: The organic iodides—(Uroselectan), Neo-Iopax (Uroselectan B), Skiodan (Abrodil), Diodrast (Neo-skiodan, or Perabrodil), Diodrast Compound, and Hippuran—as urographic media were developed with the success of excretion urography. A historical background is therefore not amiss. Rowntree and his co-workers, utilizing a 10 per cent solution of sodium iodide intravenously and by mouth, reported in 1923 the visualization of the urinary bladder and in some cases the pelvis and ureter. The following year Rosenstein and von Lichtenberg reported their results repeating the work of Rowntree and his co-workers but in conjunction with perirenal pneumoradiography. In the same year Volkmann published his observations with the use of various halogen compounds, finding the intravenous injection of a 10 percent solution of sodium iodide to be the most valuable. In 1927, Lenarduzzi and Pecco tied off the ureter in animals and injected sodium iodide intravenously

producing positive roentgenograms of the kidney pelvis and ureter. Hyrutschak, in 1928, employed a large series of bromine and iodine compounds, some of which were aromatic in nature. In some of the experiments he simultaneously employed caffeine, urea, pituitary extract, and atropine in order to influence excretion as well as the dynamics of the pelvis and ureter. Ziegler and Köhler used 10 gm. of sodium iodide and 10 gm. of urea in milk in conjunction with compression.

All the aforementioned investigators who utilized the halogen compounds found that these could not be given in sufficiently large quantities to be of any practical value for excretion urography, although under favorable conditions in occasional cases, the kidney pelvis, calyces and ureters could be made out.

The first to achieve practical results was Roseno in 1928 who used a combination of sodium iodide and urea called "Pyelognost". This compound has fallen into disrepute because of associated severe reactions, and the extremely large dose required and because the visualization, although satisfactory, was frequently poor.

In 1929, the first really successful compound for excretion urography—the organic iodide known abroad as Uroselectan and in the United States as Iopax—was presented. Subsequently the following organic iodide compounds for both excretion and retrograde urography have successfully been employed:

1. Neo-Iopax (Uroselectan B.)
2. Skiodan (Abrodil)
3. Diodrast (Per-abrodil, Neoskiodan)
4. Hippuran
5. Diodrast Compound

Procedure for Intravenous Urography: The urographic solution is injected over a period of from one to two minutes. In the routine case the first exposure is made five to ten minutes after the injection, and two subsequent ones at from ten to fifteen minute intervals. Where functional disturbances are present, additional films should be taken to determine the absence of visualization or the presence of late visualization. The only complaint registered during, and for a few minutes following, the injection is generalized warmth; occasionally transient nausea, vomiting or urticaria may be present. On the completion of the injection, compression is applied and left undisturbed throughout the period of the three exposures. In order to study trapping of the renal pelvis, a late film should be taken without the compression bag, and after the patient has been in the reversed Trendelenburg position for ten minutes.

Subcutaneous Urography: This is indicated in individuals, particularly infants with very poor veins. The fields to be injected, usually the pectoral regions, are prepared in a sterile manner, and anesthetized with 2 per cent novocain. The total dose, 7 to 10 gm. of substance in 80 to 100

c.c. of distilled water, prepared under sterile precautions, is injected dividing it equally between the two sides. No reactions, except for very slight pain at times, nor local necrosis has ever been observed. Compression is applied and exposures are made thirty, sixty and ninety minutes after the injection.

Oral Urography: To date, Hippuran is the only substance on record to have yielded gratifying results in some cases: from 10 to 15 gm. dissolved in approximately 75 c.c. of a mixture of simple syrup and elixir lactopeptone, have yielded suitably diagnostic radiograms. The only objective sensation recorded is the salty aromatic taste of the solution. Nausea or vomiting have not occurred. Satisfactory results were obtained approximately from sixty to one hundred and thirty-five minutes after administration. The patient is placed upon the X-ray table forty-five minutes after the ingestion of the solution. A moderate degree of compression is applied over the urinary bladder region and X-ray exposures are made sixty, ninety, one hundred and twenty and one hundred and fifty minutes after the oral administration of the dye. Due to the innocuousness of the procedure by the intravenous route, the time-consumption factor by the oral route, and the inconsistency of satisfactory results as compared to the former method, oral urography has not withstood the test of time.

Importance of the Application of Compression: An added factor of great importance, which has aided materially in improving the results by excretion urography, has been the application of a moderate degree of compression by means of an air-inflated rubber balloon, maintained over the urinary bladder region. The use of compression is essential in obtaining readable and suitably diagnostic X-ray pictures. Without its application, incomplete, indistinct and faint shadows are often obtained. The objection raised, that the use of compression produces an artificial dilatation of the urinary tract, does not appear to be the case. Where the normal tone of the pelvis and ureter is present, normal contours are observed; where, on the other hand, atony or dilatation of the conducting system is present, this condition is visualized. A complete obstruction with the use of the compression bag is not produced, since a bladder filling is observed despite its application prior to the administration of the drug.

General Considerations: Excretion urography has proved an invaluable aid in urologic diagnosis. However, like every other method, it is not without its limitations. The early enthusiasm of some, that cystoscopy, ureteral catheterization and retrograde pyelography would become of minor importance has been proved unfounded. These various procedures must supplement one another. Where doubt exists, cystoscopy and retrograde pyelography must be carried out. The direct visualization of the urinary bladder and catheterization of the ureters are still irreplaceable in the urologic armamentarium.

Since excretion urography depends for its success upon the functional activity of the kidney parenchyma, one should constantly be aware of the renal and extra-renal factors that determine the net result in that functional activity; for only in this manner can one properly interpret and evaluate the anatomic results obtained. The normally functioning kidney possesses the ability to excrete urographic substances in high concentration in a given short period; this may be characterized as the "thrust-excretion ability of the normally functioning kidney". It is upon this concentrating property of the kidney that the success of excretory urography depends. As a corrollary, where this concentrating power is either impaired or absent, as in the poorly functioning kidney, the roentgenologic visualization is correspondingly poor or entirely absent. Broadly speaking then, the degree of visualization depends upon renal and extra-renal factors determining renal excretion. However, in the presence of urinary tract obstruction, visualization may still be observed where the normal level of excretion required for roentgenologic purposes is low, provided that renal excretion still exists. Thus, in hydronephrosis, good visualization may still be encountered in spite of the existence of relatively little intact, functioning renal tissue. An important concept to be derived from case illustrations bearing upon this consideration is the following: that in cases of hydronephrosis, the intensity of roentgenologic shadow cannot be relied upon as a quantitative measure of healthy functioning renal tissue nor one for determining the type of therapeutic procedure. The latter will depend upon the individual case and upon the operative findings.

Again, the functional activity of the kidney may be temporarily diminished or perhaps totally inhibited as a result of either occluding lesions or trauma, although the kidney parenchyma itself be intact. The concept—temporary inhibition—is employed advisedly in cases where non-visualization of the urinary tract at one examination has been followed by the restoration of function and visualization with the removal of the causative factor. Such experiences have been observed in one case following trauma from retrograde pyelography and in another from a high occluding stone. One should therefore not always conclude that the kidney parenchyma is permanently damaged beyond repair because of the non-visualization at one examination.

In addition, instances of poor or no visualization, either bilateral or unilateral, in the presence of normal renal function as determined by excretion of indigo carmine, have been noted. These failures are difficult to explain. Perhaps, in some, the origin may be faulty technique. For one thing, I consider the application of compression important in obtaining readable and suitably diagnostic urograms.

Field of Application: Where retrograde pyelography has been contra-indicated or difficult, excretion urography has frequently shed invaluable

light. For example, in the presence of hematuria, in obstructing lesions, in cases of implanted and reimplanted ureters, in congenital anomalies, in children and in individuals in whom instrumentation is harmful, excretion urography has been very helpful, aside from the fact that it offers a bilateral urogram. It is of help particularly, in patients presenting obscure abdominal symptoms and conditions, and in the differentiation of abdominal masses where one is adverse to subjecting the patient to retrograde pyelography. Chronic pyuria, usually attributed to simple pyelitis or pyelonephritis has been found to have its origin in congenital anomalies, infected hydronephroses, pyonephroses, tuberculosis, urinary calculus or, as in one case, urinary retention due to contracture at the neck of the bladder. Moreover, the mere non-visualization of a urinary tract as a result of disease of the renal parenchyma, as in pyonephrosis, is in itself of value in the localization and in the establishment of the diagnosis when viewed together with the other clinical data.

The contra-indication to this method is uremia, for when the blood urea is high and the concentrating power of the kidney poor, the method yields few or no anatomic data and becomes not only superfluous but attended by danger.

SUMMARY

Urography represents a notable advance in the science of medicine. Its claims to recognition rest upon the precision, accuracy and rationale that it adds to diagnosis. From the historical survey outlined, and with the advent of the organically bound iodides, it is observed that urography has become a relatively safe procedure today. Excretory and retrograde pyelography should complement and supplement one another.

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